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ON THE SIGNIFICANCE OF JAUNDICE IN TYPHOID FEVER, AND ON THE HEPATIC COMPLICATIONS WITHOUT JAUNDICE.[1]

By J. M. Da Costa, M.D., LL.D.,
of Philadelphia.

During the past winter there were in the wards at the Pennsylvania Hospital a number of cases of typhoid fever that presented the peculiar and rare symptom, jaundice. It is the object of this paper to analyze these cases and to inquire into the significance of jaundice when occurring in typhoid fever, at the same time that the hepatic complications in which jaundice does not generally happen will be passed in review.

Case I.—A colored woman, aged eighteen years, was in the ward for a long time, extremely ill with typhoid fever. The course of the fever was marked by only moderate diarrhœa, but it was attended with very high temperature, the record showing temperatures of 105° and upward, and by nervous manifestations, especially delirium; the Widal reaction was decided. In this case of long-continued typhoid fever there appeared two striking symptoms: one was jaundice, the second was inflammation of the right parotid gland.

The jaundice appeared on the eleventh day of the disease, and though by the thirtieth it had greatly diminished, yellowness was still perceived in the conjunctivæ. The jaundice was not associated with any marked change in the size of the liver; if there were any, it was slightly increased, for the percussion dulness was distinctly to be detected below the margin of the ribs; the organ was painful to the touch when pressure was made over its free border, and there was general sensitiveness of the abdomen.

Subsequent to this state of things the right parotid gland gave evidence of inflammation, and became tumid and tender. The swelling at the angle of the jaw subsided without suppuration, under local

[1] Presented to the Association of American Physicians, May, 1898.

treatment with ice and applications of tincture of iodine, and by the thirtieth day of the disease there was very little to be felt of the parotid swelling, which at one time threatened to form an abscess. As further symptoms in the case may be noted nausea and vomiting, hebetude, and albuminous urine showing blood-cells and granular and hyaline casts, as well as pus casts and bile-stained epithelial cells. The urine was freely passed, forty-six ounces in twenty-four hours, and contained one-half gramme of albumin to the litre; it responded readily to the tests both for biliverdin and bilirubin. On several occasions chills occurred, but they were not severe; the blood was examined for malarial organisms, with negative results.

Jaundice persisted, though slight, for a few days more; the tenderness over the lower part of the liver disappeared; the bowels were constipated; the tongue was somewhat coated; the temperature was 99°. The urine, tested repeatedly when the jaundice was at its height, gave evidence of the presence of bile-pigment. The stools were never clay-colored; indeed, they were usually the ordinary stools of typhoid fever; sometimes they were noted as brown, sometimes as yellow, or greenish. No bile-pigment was detected in the urine on March 7th, the thirty-second day of the disease. The patient made a good, though slow, convalescence.

It is worthy of note that the jaundice was associated with parotid swelling, which I think more than a coincidence, as it has happened in other instances, as we shall further on see.

Let me now give the particulars of a case of jaundice in typhoid fever which came on very late in the disease, only three or four days before death, and grew in intensity to the fatal ending.

Case II.—Sarah K. B., aged thirty years, white, was admitted February 18, 1898, with the statement that thirteen days previously she had been taken ill with anorexia, diarrhœa, vomiting, and epistaxis. She had not had a chill, headache, or cough. Upon admission her temperature was 104°, the pulse 120, the respirations were 40 to the minute. Her cheeks were flushed, the pupils were large, the sclera clear, the conjunctivæ of a good color. Sordes existed upon the teeth and lips. The tongue was dry, red at the tips and edges, with a brown streak in the centre. Her breath was fetid. The lungs were clear on percussion; there were no râles. At the apex of the heart was heard a blowing systolic murmur, not transmitted; at the base, too, was a soft, blowing systolic murmur, which was transmitted into the carotids; there was no venous hum. The heart's action was regular, but rapid. The pulse was small in volume, and dicrotic. The liver dulness began at the sixth rib, and extended to the costal margin; the border was not palpable. The spleen extended from the eighth rib in the mid-axillary line to the last rib; it was not palpable, and not tender upon percussion. The abdomen was tympanitic, and, upon pressure, pain and gurgling were elicited in the right iliac fossa. Characteristic rose-spots were found on the abdominal surface. There was pre-tibial œdema, and some pain upon pressure in the legs.

On the following day it was noted that hebetude was marked, the facial expression was dull, the temperature was 102° to 103°, the pulse

very weak, dicrotic, and compressible. The urine was straw-colored, with an abundant sediment. It was acid, of specific gravity 1030, and contained a trace of albumin, with abundant urates and granular and hyaline casts.

The treatment was beta-naphtol, three grains every third hour; whiskey, a half-ounce every second hour; strychnine sulphate, one-thirtieth of a grain every fourth hour, and a milk diet. The surface of the body was sponged with cold water every third hour, when the temperature was 103° or over.

During the next few days the bowel movements continued loose and frequent, from four to seven daily. The eruption became more profuse. The temperature was only kept down by systematic sponging. The splenic area of dulness became much increased, and some local tenderness developed. The tongue became dry, brown, and fissured. The Widal test of the blood yielded a positive reaction. The stimulant was increased to five drachms every two hours on the 21st, on account of the very dicrotic character of the pulse; but as this was better the next day, the whiskey was decreased to four drachms every two hours. The hebetude continued. There was epistaxis on the 23d. On the 24th the pulse was noted as stronger and more regular, though still rapid. A systolic murmur, looked upon as hæmic, persisted. There was marked throbbing of the carotids; the second cardiac sound was distinct. She was weak and exhausted, at times delirious, though the mind was mostly clear. On the 25th some yellowness of the conjunctivæ was observed, and the urine contained bile-pigment. On the 26th it was noted that the skin and conjunctivæ were markedly jaundiced. The pulse was feeble and compressible. The bowels were very loose, eight movements within the last twenty-four hours, notwithstanding the use of opium suppositories; the discharges were thin and yellow. Dilute nitromuriatic acid, fifteen minims, was given every four hours in place of the beta-naphtol, which had been discontinued. Oxygen inhalations were also employed, and she took strychnine.

On the 28th the records state that the delirium was deepening. She was intensely jaundiced all over her body. The eruption was still profuse. The liver was not enlarged or palpable; there was no pain or soreness over it. The pulse was very weak. Sordes were present on the teeth and tongue. The bowel movements were green and yellow, and still loose. In spite of a very free stimulation, the patient died of exhaustion during the evening. An autopsy was not obtained.

In the cases that have been detailed the jaundice occurred as a late symptom. Jaundice may be, however, an early symptom, and even show itself in advance of the fever, appearing as the result of an early infective process in the bile-ducts.

In a remarkable case which, so far as I know, is unique, the jaundice distinctly preceded the development of the typhoid fever, and occurred during the latter part of the period of incubation.

CASE III., a Danish weaver, was admitted into my ward at the hospital on January 7, 1884. He had been jaundiced for a few days without obvious cause. He complained of weakness and loss of appetite.

His temperature was 99.5°, the pulse 118. The next day the yellowness of the conjunctivæ and the skin was more marked, the tongue had a heavy yellow coat, the liver was observed to be somewhat enlarged, as was the spleen. The case was looked upon as one of catarrhal jaundice, and he was treated with phosphate of sodium and Rochelle salts, and placed on a restricted diet. The jaundice slowly improved and almost passed away, but the man did not get well, for, after the 19th he was noticed to be decidedly feverish, and on the 24th the morning temperature was 104°, and he was very weak; his face was flushed; diarrhœa set in. A note made at this time states that he had all the appearances of beginning typhoid fever. On the 27th there was no doubt of the correctness of this view. The tongue was coated, with red edges and tips. The abdomen was tympanitic, the movements from the bowels loose and of typhoid character. Rose-colored spots were found on the abdomen. He had repeated epistaxis.

He was treated with eight grains of quinine daily, with stimulus, with dilute muriatic acid, and, later, with turpentine. In the course of the case great restlessness, delirium, and subsultus tendinum were noted, followed by marked hebetude, increasing prostration, and frequent involuntary movements from the bowels. He died February 4th, from exhaustion.

At the autopsy the liver was found to weigh four pounds and eight ounces. The gall-bladder contained thin, pale-colored bile. There was no evidence of inflammation or ulceration of its mucous membrane, or of disease of the bile-ducts. The hepatic cells showed a cloudy swelling. The same condition was noticed in the epithelium of the kidneys, which were otherwise healthy. The spleen weighed twenty ounces, was highly congested, and its tissues soft. The posterior portions of the lungs were much congested. A number of infiltrated and ulcerated Peyer's patches were found in the lowest part of the ileum. There was also ulceration of many of the glands of the large intestine, and considerable swelling of the glands of the mesentery.

It is difficult in this case to state exactly when the typhoid fever began, but, counting from the appearance of the eruption, which we know to be between the seventh and ninth days, the fever probably started on the 18th or 19th of January, and thus about two weeks after the onset of the jaundice. This, therefore, would be strictly within the period of incubation, and it seems reasonable to suppose that the typhoid infection had lighted up a catarrhal process in the gall-bladder and bile-ducts which antedated the intestinal affection and disappeared in the course of the febrile malady. The alternative suggestion is coincidence, which seems very unlikely.

The case of jaundice in typhoid fever that I shall now describe was admitted into the Pennsylvania Hospital on January 31, 1898, the day on which I gave up the men's medical ward to my colleague, Dr. Arthur V. Meigs, who kindly permits me to give the details of the case as it developed under his observation.

Case IV.—J. S., a waiter, aged twenty-six years, was admitted into the hospital with the distinct statement that he had never had

pneumonia, any affection of the liver, rheumatism, or typhoid fever. He had been ill for ten days previous to admission, and a week before his admission he was seized with a severe chill, followed by fever, sweats, and epigastric pains. From this time on, he had a number of chills, with severe abdominal pains, most acute over the region of the gall-bladder, accompanied by obstinate constipation and vomiting. When examined on admission his temperature was 102.2°, the pulse 88, the skin and conjunctivæ were decidedly jaundiced, the tongue was heavily coated, the abdomen rigid, not distended, but generally painful on percussion. There was no particular tenderness in the right iliac fossa. The greatest tenderness was over the region of the gall-bladder, and pressure there caused nausea. The liver was distinctly enlarged and palpable. A considerable amount of urine was drawn by catheter. The man lay in bed with his legs flexed and with all the appearances of a local peritonitis. Poultices were applied to the abdomen without material modification of the symptoms. On the evening of the first day the temperature attained to 104.4°. It declined to 98.6° the next morning, and then passed by evening to 103°. On the second day after admission it had fallen early in the morning to 99°. The patient was extremely restless, with clammy perspiration, the pulse was imperceptible, and he soon died.

His case suggested an inflammatory disease within the abdomen rather than typhoid fever, and the symptoms were such as might have been due to an appendicitis at the upper part of the appendix.

At the autopsy typical typhoid ulcers were found in the ileum and cæcum, the mesenteric glands were swollen, the spleen was large and friable; there was no peritonitis. The liver was considerably enlarged; its left lobe had a blunt edge. There was no abscess or gross lesion in the liver. The gall-bladder was distended with an unhealthy-looking bile; it contained no concretions; its coats were not altered; it had no adhesions. There was no swelling or sign of inflammation in the biliary ducts. The base of the right lung was congested.

It appeared at first from the symptoms that the case was one of cholecystitis; the nausea and vomiting, and especially the seat of pain, pointed to it. But the autopsy did not bear out this view, since no signs of inflammation of the gall-bladder were found. The distention of the viscus was the only thing to account for the pain; and the jaundice must, after all, have been the result of the blood alteration and the morbid condition of the liver structure. It is to be regretted that there are no microscopical or bacteriological examinations to record.

In the case we have just examined the jaundice was associated with the occurrence of chills; indeed these formed a prominent feature of the morbid manifestations. They were yet more so in the following case, though the lesion was, I believe, a different one. The man was shown at a clinic with great enlargement of the spleen in the course of typhoid fever, and the jaundice subsequently developed in the midst of very grave symptoms.

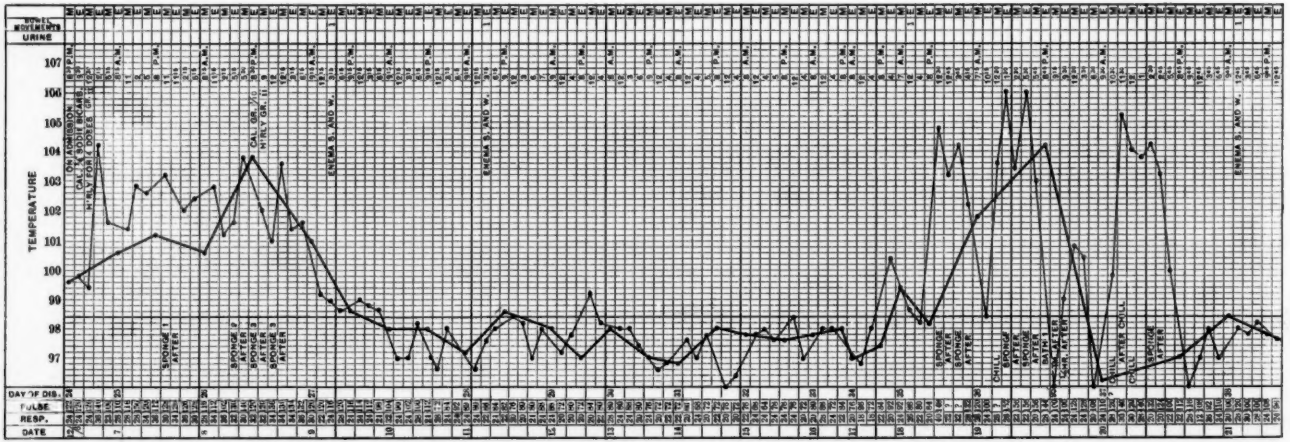
Case V.—A Swedish sailor, aged twenty-three years, was admitted on December 6, 1897, with severe abdominal pain that was at first

over the whole upper part of the abdomen, but had localized itself in the left hypochondrium, extending almost to the crest of the ileum. The temperature was 99.6°. The bowels were moved two or three times daily; the discharges were not loose. The pulse was 120, weak and irregular; the tongue markedly coated and tremulous. The history obtained was that he had been an unusually healthy man who did not remember any illness except an attack of malaria some years ago. Eight weeks since, while at sea, he began to suffer with headache and weakness; subsequently was seized with fever; was delirious part of the time, and altogether decidedly ill for weeks on board ship. He was very weak when he left the ship, but after reaching land he began to improve until the last few days, when he had night-sweats, abdominal cramps, and felt himself very ill. The day of admission the temperature rose in the evening to 104.2°; no rose-spots were found. The most marked feature of the case was the extent of the splenic dulness, which was 18 cm. in length from the sixth rib laterally, and passed fully two fingers'-breadth below the costal margin. The enlarged organ could be distinctly felt, and was very tender on pressure; indeed, the whole splenic region was tender to the touch, extremely so on percussion. Bulging was visible to the eye, and the line of dulness was influenced by inspiration and expiration. The heart's action was rapid, the second sound accentuated; there was no murmur; marked pulsation existed at the supra-clavicular notch.

He was looked upon as having typhoid fever with splenitis, and the question of abscess of the spleen was considered. There was some doubt whether we were dealing with the primary attack of the fever, prolonged by the condition of the spleen, or with a relapse; the former view was adopted. The patient was placed on dilute muriatic acid, twenty minims every fourth hour, on milk diet, and the ointment of iodide of mercury and lanolin, equal parts, with four grains of extract of belladonna was rubbed in over the spleen. The blood examined microscopically showed 4,500,000 red to 6000 white corpuscles. Widal's reaction was positive. The urine was acid, of specific gravity 1029, and contained neither sugar nor albumin, nor casts.

On December 9th, three days after admission, a crop of rose-spots was found on the abdomen. These disappeared by the 13th; his whole condition was steadily improving, and the temperature had become normal. A note on the 16th speaks of the large size of the spleen persisting, but of the tenderness having gone; of the absence of tympany, of tension of the abdomen, and of any signs of cardiac disease. On the 17th the temperature began to rise, and by the evening of the 18th it had attained to 105°; the pulse was 148, and weak; the respirations were 40. There was slight return of the splenic tenderness, but nothing marked. The blood was examined for plasmodium; none was found. Dark days followed, with recurring severe chills and temperature of 106°, with a pulse weak and 156, with hurried, shallow breathing and congested lungs, but with the murmur remaining vesicular. The first sound of the heart was indistinct, the second clearer and well defined. In the blood, repeatedly examined, no plasmodium was detected; a repetition of Widal's test gave again the same positive result. Quinine in large doses produced no effect on the chills, and but little on the temperature. A cold bath reduced it to 95°, but he did not bear the bath well. The temperature rose again by the next day to 105.3°, and

Temperature Chart of Case V.



The lighter lines represent the intermediate temperatures.

two chills happened on that day. After the chills and the fever rises the patient did not sweat, but the skin was moist. A note of the 21st mentions yellowness of the skin and the conjunctivæ, and bile in a urine free from sugar, but slightly albuminous and containing hyaline and granular casts. There was no distention of the gall-bladder; the lower border of the liver could be felt, and was slightly tender; the organ extended just below the margin of the ribs. General abdominal pain existed at the upper part of the abdomen; the stools were not clay-colored.

During the time of the chills and fever, and at the height of the jaundice, the treatment consisted chiefly in sixteen grains of quinine daily, and in borate of sodium, ten grains every third hour, given for a time in place of the dilute muriatic acid, which, however, was afterward resumed; and, while the temperature was so high, three grains of phenacetin, with two of salol, were also administered with some apparent effect. For a time, too, the weakness of the circulation necessitated the free use of digitalis and of whiskey.

The temperature, by the 21st, became normal and remained so with occasional exacerbations during convalescence. There was, however, from January 2d to the 10th, a post-typhoid temperature reaching 102°, without return of the eruption. The splenic dulness gradually decreased, and by the 5th extended merely to the margin of the ribs; the jaundice had entirely disappeared by the 5th, even to urinary tests. The man left the hospital, well, on January 26th.

It is very difficult to explain this case. As regards the spleen, there was no doubt of its great enlargement and tenderness, more marked than I have ever seen in typhoid fever, and I looked throughout the case for an abscess. But no positive evidence of this was ever obtained, and if it happened, or a purulent infarction occurred—which, as Murchison noticed in two cases, softened—the purulent fluid was absorbed or encapsulated, and no rupture took place.

Regarding the spleen as the source of the grave symptoms, two views suggest themselves to account for the chills and the jaundice. One is that they were both pyæmic from the morbid process in the spleen, the jaundice being of blood origin, as it is in pyæmia. The second is that, considering the splenic vein as a main branch that goes to form the portal vein, infected thrombi produced a pylephlebitis, and that chills and jaundice, the latter certainly, resulted from the superinduced condition of the portal vein. The difficulty of adopting this view is the recovery. Still, we know that pylephlebitis may end in recovery. Frerichs tells us that this may happen when the pylephlebitis is not too extensive. In a recent operation for typhlitis Treves[1] actually saw the morbid lesions. The liver surface was dotted over with the innumerable yellow specks regarded as characteristic of the disease, and the patient's condition appeared hopeless, but she recovered. On the whole, I believe that the view of the patient whose case I have been describing having had pylephlebitis is the correct one.

[1] British Medical Journal, February, 1894

Jaundice is of very rare occurrence in typhoid fever. Sir William Jenner[1] states that he has never observed a case. Murchison[2] has met with it in but four instances, and had a fifth case communicated to him. My friend and late colleague at the Pennsylvania Hospital, James H. Hutchinson, reviewing his experience in typhoid fever in an excellent article,[3] mentions that he had not seen this complication. Petrina,[4] during the years 1875 to 1880, met with but one case in 194 deaths from typhoid fever. Griesinger is quoted by Liebermeister[5] as having noted it ten times in 600 cases, and Liebermeister mentions that in the hospital at Basle it was observed twenty-six times in 1420 cases, or one in about fifty-five. These figures indicate higher proportions than jaundice is generally regarded as occurring in, except in hot climates. Jamieson[6] states that in China it is generally, perhaps always, present to a greater or less extent in prolonged cases, and cites nine cases in which it was deep. But Sorel,[7] in Algeria, observed only six cases in 871 of typhoid fever. In cold climates jaundice in typhoid fever must be very rare. Huss,[8] in analyzing 2294 cases of typhus abdominalis—typhoid fever—in Stockholm, does not mention an instance. Yet Werner,[9] in St. Petersburg, speaks of having observed ten cases in one outbreak of typhoid fever.

Prior to this winter I had met with but a solitary instance that I can recall, and it is remarkable that this paper, which contributes five to the scanty general number, should record four observed in the last few months, during which we have had a widespread epidemic of typhoid fever in Philadelphia. Where there is a complication of malaria, jaundice is not infrequent. Thus, in the report of so-called typho-malarial fever from the Seminary Hospital during the civil war,[10] jaundice occurred in seven out of 64 cases, only one case of which was fatal.

As regards the time of the occurrence of the jaundice, it generally does not come on until the middle of or until late in the disease. In my own cases, omitting Case III., where it antedated the febrile malady, it began in one case (Case I.) on the eleventh day; in Case II., on the twenty-third day; in Case IV. it probably came on in the first week; in Case V., as convalescence seemed to have been reached. In most of the many instances on record that I have analyzed, it appeared in the second or third week of the disease. Still the jaundice may happen

[1] On Fevers and Diphtheria.
[2] Diseases of the Liver, 2d ed., 1877, p. 401.
[3] System of Practical Medicine by American Authors, vol. i. p. 295.
[4] Prag. med. Wochenschrift, 1881, No. 41–43.
[5] Ziemssen's Cyclopædia of the Practice of Medicine, vol. i.
[6] Imperial Maritime Customs, China Med. Reports, 1888–95, 37th Issue, pp. 63, 67.
[7] Bull. et Mém. de la Société Méd. des Hôpitaux de Paris, 1889, tome vi. 3d series.
[8] Statistics and Treatment of Typhus and Typhoid Fever, etc., 1855.
[9] St. Petersburger med. Wochenschrift, 1892, p. 32.
[10] Medical and Surgical History. Medical History, part iii. p. 305.

early, as it did in many of Jamieson's cases.[1] In one of Andral's fatal cases[2] it occurred on the third day; in a fatal case of Frerichs',[3] on the fifth; in one of Murchison's[4] that recovered, it appeared on the sixth day of a relapse; in one of Osler's[5] cases, also ending in recovery, on the fourth day of a relapse; in one of Sorel's[6] cases, not until convalescence; in McPhedran's case,[7] just before convalescence. It may go on, and is apt to go on, gradually deepening until death, and may—though this is very exceptional—become dark and intense. In cases that recover the jaundice gradually disappears with the fever; yet it may persist into convalescence, as in Case I. of this paper, and even remain after the patient is able to be about.[8]

With reference to the symptoms that attend the jaundice, we do not find that they are constant; they are, as a rule, the symptoms of a severe case of typhoid fever with the usual amount of tympany and nervous disturbance. Delirium is apt to be present; yet I cannot say that it has seemed to me much aggravated by the hepatic condition, and there are intervals of clear mind even in the delirious patients, as happened in Case IV. and in Case V., in which questions are answered rationally. The temperatures are, as a rule, high, and, as the cases here presented prove, chills are not uncommon; nor are pulmonary congestions. Vomiting is a frequent but far from invariable symptom. The urine almost always contains bile, and, as in grave cases of typhoid fever, is apt to show some albumin and granular and hyaline casts. Examined by Murchison,[9] in two cases, for leucin and tyrosin, these were not found. The character of the stools is of special interest; they are much like the ordinary typhoid stools, or darker and greenish; they are very rarely clay-colored. In four of the five cases here reported they were not. But in one of Murchison's[10] cases in which jaundice happened during a relapse, the stools were noticed as clay-colored, and the same in Osler's[11] case in which jaundice appeared early in a relapse. There may be, as in one of Andral's[12] cases, marked constipation. Neither the temperature nor the pulse has appeared to me to be influenced by the occurrence of the jaundice; the temperature remains high, the pulse rapid. In some instances profuse sweats occur. The liver is generally somewhat sensitive to the touch, especially at its lower border. In the cases I have noted it was slightly enlarged or of normal size. But it has been observed to be much

[1] Loc. cit.
[2] Clinique Méd., 1834, vol. i.
[3] Diseases of the Liver, 1858.
[4] Diseases of the Liver, Case CXXXVII.
[5] Case I., Transactions of the Association of American Physicians, vol. xii., 1897, p. 380.
[6] Société Méd. des Hôpitaux, tome vi.
[7] Canadian Practitioner, March, 1891.
[8] Case XXXVIII. in Murchison, Treatise on the Diseases of the Liver.
[9] Ibid., p. 420.
[10] Diseases of the Liver, Case CXXXVII.
[11] Loc. cit., p. 380.
[12] Clinique Méd., 1834, vol. i. p. 11.

reduced, as in the case reported by Sabourin ;[1] in the case mentioned by Frerichs, the hepatic dulness was almost absent.[2]

Complications attending the cases in which jaundice is met with are not unusual. Marked pulmonary engorgement existed in Cases IV. and V. detailed in this paper. In one of Andral's[3] cases the patient died of left-sided pneumonia on the ninth day of the disease; both lungs were highly congested. In a case described by Louis[4] in which jaundice and bilious vomiting occurred, there was a purulent swelling of the right parotid; abscesses were found in the liver. In the first case of my series there was also parotid swelling, but it did not suppurate. In Sander's[5] case double parotitis followed; and the number of cases of combination of jaundice with parotitis in typhoid fever shows that it is more than coincidence. In one of Frerichs' cases,[6] too, parotitis is mentioned, but it was associated with typhus rather than with typhoid, and, therefore, cannot be, strictly speaking, considered here. In another[7] of his cases of jaundice in undoubted typhoid, profuse epistaxis preceded the jaundice, as it did in Case II. of my series. In Lannois' case[8] the epistaxis was marked and repeated; the jaundice was very intense, black. Epistaxis, indeed, bears, I think, a distinct relation to the jaundice and its intensity. In one of Murchison's[9] cases thrombosis of the femoral vein happened in a patient who had become jaundiced on the fourteenth day of enteric fever. In Freundlich's case[10] thrombosis of the scrotal veins and gangrene of the left inguinal region coexisted. He had also double croupous pneumonia of the lower lobes. When jaundice is severe and occurs early, Jamieson[11] speaks of its usual association with hæmoglobinuria, intestinal hemorrhage, and hæmatemesis —indications of blood dissolution.

Having examined into the mode of appearance of the jaundice and the symptoms attending it, let us inquire into its origin. Is it a jaundice of obstruction to the flow of bile, such as we know catarrhal jaundice to be, or is it due to the blood condition and the changes in the parenchymatous structure of the liver? In the great majority of instances, most assuredly, I think, not to the former condition. It is usually a blood jaundice, with more or less disorganization of the red corpuscles and often associated with alteration in the liver cells. In favor of this view we have these facts: its occurrence, as a rule, as a late symptom and in grave cases; the character of the stools, which are

[1] Revue de Médecine, 1882, p. 600.
[2] Observ. XVIII., Diseases of the Liver, vol. i., Sydenh. Soc. Trans., p. 215.
[3] Clinique Médicale, 1834, tome i. p. 11.
[4] Fièvre Typhoïde, vol. i., Observ. XVII., p. 111.
[5] Deutsche Klinik, 1861, p. 70.
[6] Diseases of the Liver, p. 168.
[7] Ibid., Observ. XVIII., p. 215.
[8] Revue de Méd., 1895, p. 911.
[9] Diseases of the Liver, 2d ed., Observ. CXXIX., p. 420.
[10] Deutsche Archiv. für klin. Med., Bd. xxxiii., 1883, p. 318.
[11] Loc. cit., p. 63.

but little modified, and do not show any hinderance to the flow of bile; the general similarity to the jaundice noticed in other infective diseases and altered blood states, such as in pyæmia. The condition of the liver itself does not give us much information. Yet where the organ has been carefully examined it has been found to show degeneration, granular or fatty, of the hepatic cells, that has even been likened by Frerichs to the state found in acute atrophy. Then in some instances we have abscess, though not in many, for I shall presently show that in the majority of cases abscess of the liver attendant on typhoid fever is not accompanied by jaundice. Further, we may have a pylephlebitis, with secondary changes in the hepatic tissue. However different, these causes may be all grouped together as non-obstructive jaundice—jaundice not from catarrhal obstruction of the bile-ducts. In a few instances this, however, does happen, and the records submitted in this paper prove that it is especially as a precursor to the active development of the enteric fever (as in Case III. of my own cases), or in the early stage of a relapse, that this kind of jaundice occurs.

Broadly speaking, then, the jaundice met with in enteric fever is due to the blood affection and the alterations produced by the toxins of the disease in the secreting cells of the liver, or to gross changes otherwise there induced, and only in exceptional instances to a catarrhal condition of the bile-ducts. Besides this, jaundice in typhoid fever occurs from inflammation of the gall-bladder and the morbid changes in the bile-ducts that may attend the cholecystitis. But this I only mention here to enumerate all the causes, as we shall presently examine this disease in detail.

It is apparent that jaundice in typhoid fever is not always associated with the same lesion, and that we can no more regard it as significant of any one hepatic disorder than we can jaundice met with in the varied diseases of the liver and bile passages, unconnected with typhoid fever. Further on, I shall endeavor to make clear in how far we can, with reasonable certainty, distinguish between the different causes of jaundice in typhoid fever; but for the present I again state that the most frequent cause is from the blood infection, and without gross organic lesion; though in a moderate proportion of cases this exists.

Taking this general view of the subject, let us inquire into the gravity of the symptom. It is, indeed, a grave symptom, as may be judged from this table, in which I have placed, together with my own cases, those in which there is sufficient detail to make them of any clinical value, and excluding the cases associated with perforation of the gall-bladder and other very marked gall-bladder lesions, which I shall speak of separately.

We have thus, in 52 cases, 33 deaths and 19 recoveries. Analyzing

further these cases, according to their probable cause, we find them thus grouped: 4 catarrhal; 3 pylephlebitis, of which in one (the case of McPhedran) there were also marked changes in the liver; 5 of cholecystitis, in 2 of which (the cases of Sander and of Griesinger) there was most probably, too, cholangitis; 6 cases of abscess of the liver; 5 of acute yellow atrophy or a state closely akin to it (2 of Frerichs, 2 of Murchison, and 1 of Sabourin), and 29 cases in which blood infection and more or less of a fine parenchymatous change in the liver existed; of these, 5 (Sorel's) are not fully enough reported to be at all certain as to the cause of the jaundice, and, for the sake of accuracy, cannot be counted, leaving 24 in which the condition just mentioned was either proved or may be with reasonable certainty assumed to have existed. It would be very desirable to separate those in which there is a mere blood infection, induced by the presence of the typhoid bacilli or their toxins in the blood, or the absorption of septic matter with or without infected thrombi, and leading to alterations in the blood-corpuscles, from those in which decided, though not gross, parenchymatous changes happen. But it is impossible to do so with any certainty. Moreover, there is no fixed line; changes in the liver texture are soon secondarily induced.

Looking at the results, according to the best-ascertained cause of the jaundice, we note in the four catarrhal cases three recoveries and one death, this being the catarrhal case of my series, which, however, died a considerable time after the disappearance of the jaundice. In the three cases of pylephlebitis we find one recovery and two deaths; in the five cases of cholecystitis with jaundice there were two recoveries and three deaths; in six cases of abscess of the liver, one recovery and five deaths; of the five cases of yellow atrophy all died.

The most common of the ordinary and lighter changes in the liver structure consists in a cloudy swelling, with granular degeneration in the hepatic cells. But Handford,[1] while mentioning that both parenchymatous and interstitial changes are frequently found, regards as the most constant and, perhaps, the most important of these, interstitial hepatitis. This may, as a sequence, lead to atrophic cirrhosis, as in a case reported by Bourdillon.[2] The little opaque areas of destroyed liver-cells, that were formerly described as lymphoid nodules, and are not uncommon, do not, so far as is known, give rise to any symptoms pointing to the necrotic change.

The question may arise whether the jaundice may not be due to some agent employed in the treatment. But it has been observed under the most diversified, including the cold bath, treatment.[3] Werner,[4] who

[1] Hepatitis in Enteric Fever. Trans. Path. Soc. London, 1889.
[2] La Semaine Médicale, September 30, 1891.
[3] Goltdammer mentions two such cases. Deutsch. Arch. f. k. Med., 1877, Bd. xx. p. 68.
[4] St. Petersburger med. Wochenschrift, 1892, p. 32.

is an advocate of the use of chloroform in typhoid fever, states that he observed jaundice in four cases, very light in three, without swelling or tenderness of the liver, and stopped the remedy. But in six other cases treated with chloroform later, also in boys under fifteen years of age, notwithstanding the longer use of the remedy, jaundice did not occur.

Jaundice in typhoid fever happens most often at the *age* at which typhoid fever usually happens. But Petrina[1] reports a case in a woman aged fifty-six years; Burder,[2] one in a boy aged nine years. I do not know of a single instance in early childhood. As regards *sex*, many more cases have been met with in men than in women.

The main object of this paper is the consideration of the clinical significance of jaundice in typhoid fever, and this has now been done. But it would be incomplete without inquiring into the frequency with which jaundice is absent, though hepatic complications exist, and without a consideration of the character of these complications. Of the relative importance of these, we may get a fair idea by examining Hölscher's statistics in 2000 fatal cases of typhoid fever at the Pathological Institute of Munich.[3] Among 227 involving the liver and gall-bladder, there were 203 of disease of the liver structure; 12 cases of abscess; 3 of acute yellow atrophy; 1 of amyloid degeneration of the liver; 5 of diphtheritic processes in the gall-bladder and suppuration, including one of perforation of the gall-bladder; 3 of œdema of the gall-bladder; while 22 in addition are classed simply as icterus, without being linked to any organic disease.

The ordinary parenchymatous alterations that are presumably represented by the 203 in the numbers just quoted, are not to be recognized during life, and force themselves on our attention only in the few instances in which they are attended with jaundice; the very great majority of the changes in the liver structure in typhoid fever give rise, indeed, to no symptoms. Leaving for separate consideration diseases of the gall-bladder, *abscess* of the liver is the affection which most often manifests itself. Yet it cannot be said that abscess of the liver in typhoid is often met with. Hölscher's statistics have just been quoted. Romberg mentions 677 cases with 88 deaths, among which there was but one liver abscess; it was associated with suppurative pylephlebitis. Schultz[4] analyzed 3686 cases with 362 deaths, without a single instance of hepatic abscess.

As regards abscess of the liver, I have collected twenty-two cases in which the association with typhoid fever seemed beyond doubt, and

[1] Prager med. Wochenschrift, 1881, Nos. 41 and 43.
[2] Lancet, October 17, 1874, p. 552.
[3] Münchener med. Wochenschrift, January, 1891, Nos. 3 and 4.
[4] Observations made at the Hamburg Hospital, quoted by Romberg, loc. cit.

which admit of more or less complete clinical analysis. Others that have been reported I have rejected as very uncertain, as the combination with typhoid fever is not proved. Bouillaud's case, mentioned by Andral,[1] which has been questioned, I have included. Of the 22 cases, 7 only had jaundice; in 3 it is specifically mentioned as not present, and in 12 it is not mentioned at all, making 15 cases out of 22 in which jaundice may be fairly presumed to have been absent. Thus jaundice is not a symptom to be depended on in the diagnosis of abscess of the liver in typhoid fever. More important are chills, violent, prolonged, and repeated, as in Barth's[2] case, and generally preceding the jaundice, should this happen, as in Romberg's case; great variations in temperature, as in Case I. of Petrina; profuse sweating and sensitiveness in the region of the liver. The liver may or may not be swollen; in Goltdammer's case it was swollen. In Gerhard's case[3] the right hypochondrium was prominent, and tender on pressure, and fluctuation was detected over the right lobe of the liver. As further symptoms pointing to abscess of the liver, should there be any hepatic manifestations, are abscesses in other parts of the body, as in the parotid (Louis's case); in the perichondrium of the larynx (Chvostek's case); over the mastoid region (Sidlo's case). At times hepatic symptoms are wholly wanting, and the abscess is only found at the autopsy.

All the symptoms mentioned may also happen in pylephlebitis, except the rarest, fluctuation; especially the repeated chills, the pain and tenderness in the hepatic region, the high irregular temperature; and I know no way of distinguishing pylephlebitis from abscess, with which, indeed, it is generally classed, unless by the progress of the case, in which enlargement of the subcutaneous abdominal veins and collections of fluid in the peritoneum may be observed in addition. But the latter signs occur to a decided extent only where there is also marked thrombosis in the portal veins or its main branches, as in a case of Lannois,[4] and there is apt to be painful enlargement of the spleen as well as of the liver. I think jaundice, most probably pyæmic and from infected thrombi, is apt to happen among the symptoms of pylephlebitis with greater frequency than in abscess of the liver not associated with this, and to become deeper; but it is far from invariable. It was absent in the case of Asch and of Bernhard,[5] an instance of pylephlebitis from suppurating glands in the mesentery, and where there was a purulent thrombosis of the mesenteric veins and the venæ portæ were full of pus.

[1] Clinique Méd., 3d edition, 1834, vol. i. p. 616.
[2] Bull. de la Soc. Anat., 1853, p. 80.
[3] Medical News, July 24, 1886.
[4] Revue de Médecine, 1895, p. 913.
[5] Berlin. klin. Wochenschrift, 1882, xiv. p. 772, and Jahrb. für Kinderheilkunde, N. F., 1886, Bd. xxv.

TABLE OF FIFTY-TWO CASES OF JAUNDICE OBSERVED IN TYPHOID FEVER, WITH RESULTS.

No.	Author.	Reference.	No of cases.	Probable cause of jaundice.	Marked associate symptoms.	Result.	Post-mortem appearances.	Remarks.
1	Andral	Clinique Médicale, 1834, vol. i. pp. 10, 616.	2	Blood infection	In the first case pneumonia of left lung; heavy congestion of both lungs. In the second case jaundice very marked.	Died.	In both cases lesions of typhoid fever; condition of liver not stated in first case. In second nothing abnormal was seen in liver and biliary passages.	
2	Louis	Fièvre Typhoïde, 1841, vol. i. obs. xvii. p. 118, and obs. xxvi. p. 369.	2	Blood infection and liver abscess in first case; blood infection in second case.	In the first case suppurating parotid gland; pain in the sides and in epigastrium; bilious vomiting; marked delirium. In the second case jaundice on the twenty-fifth day of the disease, preceded by erysipelas of leg.	Died.	Typhoid fever lesions in intestines; enlarged mesenteric glands; an abscess near the free border of the liver; six smaller masses (metastatic abscesses?) in the small and middle lobes; bile passages healthy. In second case many typhoid fever ulcers; softened mesenteric glands; healthy liver and biliary ducts; distended gall-bladder.	
3	Frerichs	Diseases of the Liver, obs. xiii., 1858, obs. xviii.	2	Blood infection and parenchymatous change in liver (like acute yellow atrophy).	Great tenderness in region of liver, and afterward of entire abdomen; thin greenish stools; bilious vomiting: chill, dyspnœa. In the second case chill; thin, pale stools; violent epistaxis; tremor; dyspnœa; diminution of hepatic dulness.	Died.	Typhoid ulcers in ileum; débris of disintegrated cells, oil globules in the portions of softened liver; liver yielded lucin and tyrosin abundantly; gall-bladder not affected. In the second case liver shrivelled; disintegrat'n of hepatic cells, some filled with fat; mucous membrane of gall-bladder not affected; small quantities of whitish fluid in gall-bladder.	
4	Sander	Deutsch. Klin., 1861, p. 70.	1	Cholecystitis and probably cholangitis.	Jaundice appeared at end of second week; became very marked; vomiting; grayish stools; severe pain like bilious colic; tenderness in hepatic region and enlargement of liver; after five or six days gradual disappearance of the jaundice.	Died.	Biliary ducts were found to be dilated, and a large number of stones were in the gall-bladder.	After having entered on convalescence, the patient died in the eighth week subsequent to double parotitis.
5	Chvostek	Med. Chirurg. Rundschau, June, 1864, p. 188.	1	Blood infect'n; liver abscess.	Laryngeal perichondritis; deep jaundice; abscess of lung; pneumothorax.	Died.	Two large abscesses in liver, evidently pyæmic and secondary; also abscess in left lung.	

6	Burder	Lancet, Oct. 17, 1874.	1	Blood infect'n; liver abscess.	Icterus on sixth day of fever in a boy nine years of age; greatly increased after a chill on the eighth day; liver dulness normal; diarrhœa.	Died.	The liver was a mass of small abscesses; superficial ulceration of Peyer's patches.	Had the bath treatment; death on seventeenth day of the disease.
7	Heitler	Wien. med. Presse, 1875, No. 3.	1	Blood infect'n; parenchymatous change in liver.	Date of beginning of fever uncertain; jaundice probably about third week, preceding diarrhœa; stools bilious, subsequently yellow; no chills; urine albuminous, also blood and tube-casts in it; normal liver percussion; increasing jaundice; delirium; coma.	Died.	Ulcers in ileum; lungs congested; liver rather large, flabby, soft; brown bile in gall-bladder; spleen enlarged to four times its normal size.	
8	Sidlo	Der Militär Arzt., Wien, 1875, No. 23, p. 20.	1	Abscess of liver.	Pain in the hepatic region on thirty-second day of typhoid fever; on thirty-fifth day jaundice; swelling of liver; abscesses over right mastoid, in right temple, and in right axilla; tumor there gradually shrank; great emaciation; gradual diminution of liver dulness and of jaundice.	Recov.	.....	Abscess of liver discharged through bowel, pus and blood passing by the bowel on eighty-fourth day, after severe abdominal pain; complete recovery by one hundred and twentieth day.
9	Griesinger	Infectionskrankheiten; detailed also by Hagenmüller, Thèses de Paris, 1876, No. 269.	1	Cholecystitis with probable cholangitis.	Woman, aged twenty, in sixth week of typhoid fever, peritonitis, icterus, chills; painful tumor to right of umbilicus; swelling of liver; great prostration; convalescence. In eighth week return of tumor, with chills; icterus, vomiting; got better; subsequently two more relapses; the symptoms disappearing under treatment with large doses of opium. Final recovery in fifth month.	Recov.	.....	The patient had previously had jaundice several times, especially at her periods. The case is remarkable for its length, the recurrence of the symptoms, and the final recovery.
10	Laveran	Case communicated to Hagenmüller and published by him, Thèses de Paris, 1876, No. 269.	1	Cholecystitis.	Repeated bilious vomiting, severe pain in right hypochondrium, which is painful; icterus slight; fever reaching 40.6° C.; considerable prostration; no tumor mentioned.	Recov.	....	Symptoms came on in sixth week, early in convalescence.
11	Goltdammer	Deutsch. Arch. f. k. Med., 1877, vol. xx. p. 68.	2	First case most likely from blood infection and parenchymatous change. Second, catarrhal; but not fully enough reported to be certain.	Tenderness and swelling in hepatic region in one case of severe typhoid fever; no details given of second case except that the jaundice was of short duration and occurred in convalescence.	Recov.	.....	Very meagre details given. In both cases the bath treatment had been employed.

No.	Author.	Reference.	No. of cases.	Probable cause of jaundice.	Marked associate symptoms.	Result.	Post-mortem appearances.	Remarks.
12	Murchison	Diseases of the Liver, 2d ed., 1877, Cases CXXXVII., CXXXIX. Two mentioned (p. 401) without being described. One case(under Rostan's care) communicated (CXXXVIII.).	5	One catarrhal (CXXXVII.); one blood infection (CXXXIX.); in the other two blood infection & parenchymatous changes; in the communicated case this also most likely cause.	In first case clay-colored stools; no hepatic tenderness; constipation; jaundice occurred in a relapse; case recovered. In Case CXXXIX. jaundice appeared on fourteenth day associated with albuminuria, subsequent thrombosis, jaundice passed away; death from gradual exhaustion. In two cases no particulars. In communicated case jaundice persisted during convalescence.	3 died. 2 recov	In two cases liver found to be small, and its secreting cells loaded with oil.	
13	Petrina	Prag. med. Wochen., 1881, Nos. 41–43.	4	Case I. Blood infection, pylephlebitis with thrombi, miliary abscesses in liver.	Severe typhoid case; jaundice appeared thirteenth or fourteenth day of disease, not preceded by chill, and gradually increased, becoming very deep; fever high (highest 40.6° C.), with marked morning remissions and evening exacerbations; profuse sweating; moderate meteorism; liver enlarged and sensitive, left lobe especially; stools yellowish-brown or brown; profuse diarrhœa toward end; bile-pigment but no albumin or sugar in urine.	3 died. 1 recov	Fresh and old cicatrizing lesions in Peyer's patches; lungs congested; liver very large, full of yellow points, which are found to be miliary abscesses; granular and fatty changes in hepatic cells; thrombosis of some of the finer portal veins; dark bile in gall-bladder; spleen large; in pancreas a few yellow foci; lungs congested.	
				Case II. Blood infection, probable parenchymatous change in liver.	Icterus eighteenth day of disease; repeated chills; marked fluctuation between morning and evening temperature; liver enlarged; whole region sensitive; vomiting and epigastric pain; profuse sweats; no albumin in urine; ascites; congested lungs, œdema of lungs.	.....	.....	No autopsy. The marked gastric symptoms and the occurrence of ascites are remarkable features of this case, which was probably one of pylephlebitis.
				Case III. Probable parenchymatous change.	Jaundice on fifteenth day, preceded by chill on thirteenth; abdomen sensitive, especially liver region over left lobe; liver increased in size; urine contains bile-pigment, no albumin; chills recur. Patient left the hospital improving, but still jaundiced; the liver and spleen were still swollen after nearly four weeks.	.....	.....	Though not specifically stated, it is likely that this patient recovered.

				Case IV. Cholecystitis, with cholangitis; interstitial hepatitis.	Jaundice on second day of a typhoid fever relapse; jaundice preceded by chills; liver enlarges, becomes tender on pressure; bilious stools, subsequently yellow; repeated chills; apparent recovery, except slight jaundice and enlarged liver remaining. Returns to hospital, a little over a month after leaving it, with œdema of lower extremities; yellowish, liquid stools; urine full of bile-pigment; general dropsy develops, with hydrothorax and ascites, and abdomen is tapped; dies of œdema of the lung after a lingering illness.	.....	Cicatrized Peyer's patches; thickening of mucous coat of gall-bladder; peritoneal adhesions between stomach and liver; liver small, surface granular; biliary ducts in liver filled with brownish-yellow masses, some containing spear-shaped concretions, others fibrinous coagula; some of the smaller bile-ducts have undergone obliteration with increase of connective tissue; this process also spread to Glisson's capsule, and led to atrophy of the liver; thus interstitial hepatitis had occurred following inflammation of gall-bladder and bile-ducts; cholelithiasis accedens is also recorded.	
14	Sabourin	Revue de Méd., 1882, p. 600.	1	Parenchymatous change (acute yellow atrophy).	Man, twenty-nine years of age; deep jaundice preceded by epistaxis; time of appearance of jaundice uncertain; meteorism, diarrhœa, delirium, albuminous urine, intestinal hemorrhage; average temperature 39° to 40.6° C.; pain on pressure in right iliac fossa and right hypochondrium.	Died.	In intestines ordinary typhoid fever lesions; heavy congestion of lungs; liver diminished in size in a state of acute atrophy with fatty degeneration of the hepatic cells; gall-bladder contained a small amount of almost healthy-looking bile.	
15	Stedman	Med. and Surg. Rep., Boston City Hospital, 3d ser., 1882.	1	Parenchymatous change in liver.	Jaundice probably early in second week; tenderness in right hypochondrium; no epistaxis, nausea, or vomiting; urine, besides bile-pigment, contains a trace of albumin; diarrhœa, hypostatic congestion of lungs; highest temperature recorded 102°.	Died.	Liver enlarged and of nutmeg appearance; Peyer's patches swollen, not ulcerated; spleen softer but small; kidneys enlarged and in a state of cloudy swelling.	This case is not free from doubt as one of typhoid fever. Death occurred on the eighteenth day, and Peyer's patches should then have shown ulceration.
16	Freundlich	Deutsch. Arch. f. klin. Med., 1883, Bd. xxxiii. p. 318.	1	Blood infect'n; pyæmia.	Jaundice early in fifth week of typhoid fever, in which thrombosis of the scrotal veins followed by gangrene there and in the inguinal region had arisen; repeated chills; in the progress of the case persistent albuminuria and intestinal hemorrhages.	Died.	Anatomical lesions of enteric fever in intestines; double croupous pneumonia of lower lobes; condition of liver not stated.	Death in middle of fifth week.
17	Mathieu	Revue de Med., July, 1886, vol. vi. p. 633.	...	.....	.....	.....	....	Very doubtful case, in which at end of the second week temperature became 38° C. Was it abortive typhoid followed by a relapse?

No.	Author.	Reference.	No. of cases.	Probable cause of jaundice.	Marked associate symptoms.	Result.	Post-mortem appearances.	Remarks.
18	Sorel	Bull. et Mém. de la Soc. Méd. des Hôpit. de Paris, 1889, vol. vi. 3d ser., p. 224.	6	Cannot judge from slight description.	Four cases happened at beginning of the malady, two of which were fatal; one case jaundice shortly before death; one in convalescence. In one case, p. 239, epistaxis was frequent.	3 died. 3 recov	.....	No particulars given, except that in one case in which there had been also bloody urine, the liver was said to have been altered.
19	Romberg	Berlin. klin. Wochenschrift, March, 1890.	1	Blood infect'n; thrombosis of vena porta, and small liver abscesses.	Intestinal hemorrhage; albuminous urine; chill on twenty-fourth day of the disease; next day jaundice; brownish or yellow soft stools, sensitive abdomen, increased liver dulness and tenderness in hepatic region; fever with irregular remissions; icterus became intense; repeated chills. Death on thirty-first day of disease.	Died.	Many typhoid ulcers, for the most part in the process of healing; phlegmonous suppuration in mesentery near cæcum; thrombi in iliocæcal veins and its branches; liver markedly enlarged and full of small abscesses, especially of left lobe; masses of staphylococci in thrombi in portal veins.	
20	McPhedran	Canadian Practitioner, March, 1891.	1	Blood infection and parenchymatous change (diffuse pylephlebitis).	Symptoms came on, in a man, as convalescence was about to set in; temperature became irregular; recurring chills with sweating; jaundice; increase of liver dulness. Subsequently signs of chronic peritonitis.	Died.	At autopsy, diffuse pylephlebitis and chronic purulent peritonitis found; in the mesentery a small abscess apparently originating in a mesenteric gland.	
21	Jamieson	Imperial Maritime Customs, China Med. Reports, 1888–95, 37th issue, pp. 63, 67.	9	Blood infection with probable parenchymatous change.	Jaundice appeared in one case on the fifth day, in one on the eighth, in three on the tenth, and one respectively on the eleventh, fourteenth, seventeenth, and forty-fourth days; deep jaundice in all, and symptom not of gradual onset.	4 died. 5 recov	.....	Four of the five cases in which jaundice appeared before the eleventh day proved fatal. Severe intestinal hemorrhage occurred in three of the fatal cases.
22	Lannois	Rev. de Méd., 1895, p. 911.	1	Parenchymatous change; cholecystitis.	Icterus began toward third week of severe typhoid fever; at first light, it became very intense, black; liver greatly enlarged, marked meteorism, intense pulmonary congestion. Death eleven days after appearance of icterus; not long before, a superficial abscess appeared on back of hand, and one on the internal surface of the leg on the same side.	Died.	Many Peyer's patches involved. Enormous liver, weighing 3000 grammes, yellow and fatty; gall-bladder greatly distended, containing, besides a clear liquid, flocculent muco-pus; superficial erosions in membrane; biliary passages, no ulceration or abscesses.	This is a very marked case of suppurative cholecystitis.

23	Osler	Transactions of Association of American Physicians, 1897.	2	Catarrhal in first case; blood infection (with parenchymatous change?) in second.	In the first case nausea and vomiting came on early in a relapse of typhoid fever, of which the original attack was one of moderate severity; jaundice appeared fourth day of relapse; no enlargement of liver; tenderness on deep pressure in front of tenth rib; nausea and vomiting prominent symptoms; profuse sweats; clay-colored stools; temperature range from 102° to 103.5°. In second case severe attack of typhoid fever; jaundice at end of second week; jaundice became of considerable intensity; meteorism; abdomen not tender; liver dulness not decreased; marked delirium; nystagmus; temperature, which had been high (105°), dropped to 97.2°.	1 recov 1 died.	.....	In the second case the patient died on the sixteenth day. It was remarkable that, notwithstanding a falling temperature for four days, the pulse was of good volume.
24	Da Costa	Present paper.	5	1 catarrhal; 1 pylephlebitis; 3 parenchymatous changes in liver with blood infect'n.	Detailed in present paper. Jaundice marked in all.	3 died. 2 recov	....	All were severe cases of typhoid fever.

Viewed in its clinical bearings, we find abscess of the liver in typhoid fever under these conditions: as metastatic abscess, due to a pyæmic infection from other parts of the body, as the consequence of pylephlebitis, which is nearly always caused by an infection from typhoid lesions in the intestine, or from suppurating mesenteric glands and a resulting infective thrombosis; or, as owing to typhoid ulceration in the biliary passages and secondary suppuration. The first of these causes is illustrated by most of the cases in the table, notably by those of Louis, of Chvostek, of Sidlo, of Dunin,[1] of Barth.[2] To the second category belong the cases of Lannois, of Osler, of Romberg, of Gerhard,[3] of Tüngel,[4] in which pus from a suppurating lymphatic gland near the cæcum broke into a root of the superior mesenteric vein; of Bückling[5] with a similar history; of Asch and Bernhard,[6] where there was also a suppurating mesenteric gland. Cases belonging to the third group are the rarest. A very striking one is mentioned by Klebs,[7] in which a suppurative inflammation of the bile passages within the liver happened, and their dilatation formed abscesses filled with thick, greenish, muco-purulent liquid. In the pus from liver abscesses, typhoid fever bacilli were found by Lannois. It may be also a question whether in some of the cases regarded as metastatic there have not been separate foci of inflammation and suppuration due to the typhoid bacilli; for instance, in the cases in which the parotid glands, as well as the liver, have been implicated.

In this connection we may discuss whether there be a form of typhoid fever in which liver symptoms arise, including jaundice, owing to the direct action of the specific micro-organisms on the liver or the bile channels. Mathieu[8] describes, under the title of "typhus hepatique benin," a case which he believes to have been of this character, and in which a relapse similar to a typhoid fever relapse happened, and Pfuhl[9] cites nine cases that came on after swimming repeatedly in a swimming school in the infected Elbe water at Altona near Hamburg, and all of which had fever and jaundice. I have analyzed these cases, and do not find their clinical history closely corresponding to typhoid fever. They all recovered, and are spoken of as due to mixed infection. Mathieu's case also recovered; and, as these cases happened before the introduction of the Widal test, we must remain in doubt as to their nature. I had at the Pennsylvania Hospital last year a case of jaundice in a colored woman (Case No. 2775), with fever, violent epistaxis, hebetude, diarrhœa, and albuminous urine, in which the

[1] Deutsch. Arch. f. k. Med., 1886, Bd. xxxix. p. 379.
[2] Bullet. de la Société Anat., 1853, p. 80.
[3] Loc. cit.
[4] Thierfelder, Ziemssen's Handb., Bd. viii. p. 84.
[5] 36 Fälle von Leberabscess, Berlin, 1868.
[6] Loc. cit.
[7] Handbuch der Pathol. Anat.
[8] Revue de Méd., July, 1886.
[9] Deutsch. Milit. Arztl. Zeitsch., 1898, vol. xvii. pp. 9, 10.

Widal test gave positive reactions. She had been suffering with fever for two weeks, and it preceded the jaundice. The case proved fatal in the third week of the disease, and seemed to be an undoubted one of typhoid fever with hepatic complication. At the autopsy no lesion was found in the intestinal glands. The mesenteric glands were here and there enlarged, and one appeared as if it had pressed upon the choledoch duct; the gall-bladder was much distended, and its mucous coat inflamed; the liver was small and in a high state of fatty degeneration; the spleen was small; the kidneys large, with signs of interstitial nephritis. Unfortunately, through a misunderstanding, no cultures were made from the liver and gall-bladder, as had been intended, and, notwithstanding the positive character of the Widal test, I hesitate greatly to bring forward the case as one of hepatic typhoid without intestinal lesion; it may have been one of acute yellow atrophy, of which it presented also many of the symptoms.

More common in typhoid fever than diseases of the liver itself are the diseases of the bile passages. We know through recent researches how frequent is their infection, especially the gall-bladder infection, with the typhoid bacilli. Chiari[1] reports the results of autopsies in twenty-two patients, and only in three was the bacillus absent from the gall-bladder. In twelve cases there was inflammation of the mucosa alone; in one the whole wall was affected, causing peritonitis.[2] In the discussion that followed a valuable paper by Mason,[3] on "Gall-bladder Infection in Typhoid Fever," Councilman stated that he had found the typhoid bacillus in nearly every case. Gilbert and Girode[4] demonstrated the presence of the typhoid bacillus in suppurative cholecystitis. Dupré[5] got pure cultures of typhoid bacilli from the gall-bladder of a patient operated on for gallstones six months after typhoid fever; in another case, in a man who died about the fifteenth day of typhoid fever, although the gall-bladder presented no obvious pathological changes, pure cultures of Eberth's bacillus were obtained.

Not only do these gall-bladder infections happen in the course of typhoid fever in association with the characteristic intestinal lesions of the disease, but they have been observed when these are absent. Cases of the kind are reported by Guarnieri[6] and in a most interesting paper by Osler.[7] Mark Richardson's[8] case, in which there was no distinct history of typhoid fever, but in which the typhoid bacillus was found in the fluid obtained from the distended gall-bladder by operation, is

[1] Eleventh Intern. Med. Congress, Zeitschr. f. Heilkunde, 1894, Bd. xv. S. 199.
[2] Case described, Prager med. Wochenschrift, 1893, No. 22.
[3] Transactions Assoc. American Physicians, 1897.
[4] Mém. de la Soc. de Biologie, 1890 and 1893. [5] Infections Biliaires, 1891.
[6] Contrib. alla patog. della infez. biliari.; also, Baumgarten's Jahresbericht, 1892, S. 234.
[7] Trans. Assoc. American Physicians, 1897.
[8] Boston Medical and Surgical Journal, December 16, 1897.

another case in point. It is quite as likely that the infection of the gall-bladder occurs in these instances through the typhoid bacilli in the blood as by direct infection from the continuous intestine. Further, great interest is attached to these gall-bladder infections in typhoid fever from the now established fact that they lead to the formation of gallstones; as, on the other hand, gallstones seem to invite the bacillary infection to the gall-bladder. The association with gallstones is curiously illustrated in a case by Chantemesse,[1] in which living typhoid bacilli were found in a gallstone removed by operation eight months after an attack of typhoid fever. Van Dungern's[2] case of bacilli found fourteen years and a half after typhoid fever in the pus from an abscess formed around the gall-bladder is unique; here, however, no stones were detected. The patient recovered.

Now, from the frequency, it might almost be said constancy, with which infection of the gall-bladder happens in typhoid fever, it would be supposed that symptoms referable to it are very common. But it is just the reverse. In the cases of irritation or the lighter cases of inflammation produced by it, there are absolutely no symptoms; even in the more severe cases, in which obvious lesions are found, symptoms are often absent or, at least, not recognizable; and thus the majority of cases pass undiscovered and mostly unsuspected. It is only the very marked ones, and chiefly those in which perforation has happened, that have been noticed. I shall attempt an analysis of such of the cases as have been published with sufficient fulness to give real information, and which seemed to me to be undoubtedly linked to typhoid fever, for it is astonishing in how many instances the evidence concerning this is most meagre. I have been greatly aided in the task by the courteous permission of Dr. Westcott to make use of the references he had prepared for the remarkable work of Dr. Keen, *On the Surgical Complications and Sequelæ of Typhoid Fever*, and by the most efficient assistance of Dr. Woodbury. After rejecting all the doubtful cases, I got together and tabulated fifty-three cases of cholecystitis in typhoid fever, some simple though marked, some suppurative, some perforative. But before analyzing these, it may be well to inquire in what proportion these affections have been noticed by pathologists, irrespective of, as well as with, typhoid fever. Courvoisier[3] gives us valuable information on this point. Of 16 cases of cholecystitis of catarrhal origin or with beginning suppuration, fully 5 occurred in the course of typhoid fever. Six cases out of 55 of empyema of the gall-bladder were due to infection, one of which was from typhoid; 41 were due to cholelithiasis. In 7 cases of phlegmonous infiltration of the walls of the gall-bladder, typhoid was twice the cause, and the other 5

[1] Traité de Méd., Tome 1, p. 764. [2] Münch. med. Wochenschrift, 1897, No. 26.
[3] Casuist. Statistiszche Beiträge z. Path. u. Chir. der Gallenwege, Leipzig, 1890, pp. 76–94.

cases were due to cholelithiasis. Fatal result is the rule in purulent cholecystitis. Of 82 cases, 53 proved fatal. Among these were 10 cases due to typhoid. In many of the cases there was no suspicion of cholecystitis prior to the autopsy. In cases of perforation of the gall-bladder, with encapsulation into the abdominal cavity, mentioned by Courvoisier, there were four in which no calculi existed, and which were due to typhoid.

Cholecystitis in typhoid fever, when at all marked, is a grave complication, no matter what be its exact form. In 58 cases of typhoid cholecystitis I have collected, there were 39 deaths and 15 recoveries, while in 4 the result was uncertain or not stated. Of the different forms, the instances of perforation without operation are the most fatal; 1 only out of 24 recovered by a discharge through the abdominal walls (case of Salzman); 3 recovered after operation (cases of Alexieef, Williams and Shield, Osler and Halsted). In suppurative cholecystitis there are a number of recoveries, but also as the result of operation (cases of Caspersohn, Mason, Richardson, Williams and Shield, Osler and Halsted). In the cases of cholecystitis which are catarrhal, recovery is not infrequent; where there is also cholangitis (as in Case IV. of Petrina and in Sander's case), the prognosis is not good. But Griesinger's case, in which this complication probably existed, recovered.

To proceed now with the clinical analysis of the 53 cases I have collected, to which, for some purposes, I shall add the 5 of cholecystitis with jaundice detailed in the table printed in this paper. Of these 58 cases there were 22 in which perforation of the gall-bladder happened. In 6 of the 22 cases of perforation gallstones were found, while in 16 they are either stated to be absent or are not mentioned; thus gallstones were not encountered in more than about one-fourth of the cases of perforation. Suppurative cholecystitis may, from the descriptions, be recognized in 24 of the 58 cases; and in eight of these was also perforation. In the other instances the lesion was catarrhal, with very slight if any suppurative change. Ulcers of the gall-bladder cannot be absolutely separated from suppurative cholangitis, as in nearly all instances some suppuration coexists.

As regards *sex*, there is very little difference in the occurrence of the marked gall-bladder complications of typhoid fever. In 48 cases in which the sex is mentioned 26 were males, 22 females. The affections may be met with at almost any *age*. In 48 cases 8 were twelve years of age or less; 40 cases were over twelve years of age. The youngest case happened in a girl, aged five years (case of Alexieef[1]); the oldest in a man, aged sixty-seven years (case of Anderson[2]).

[1] Journ. Dietskaya Med., 1896, No. 4; abstracted in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, October, 1897, p. 466.

[2] Medical News, August, 1896.

The question of the *diagnosis* of these gall-bladder complications, and the possibility of telling them apart, is of great importance. It has been stated already that in many instances they are latent, and have only been discovered after death. But the knowledge of their occurrence, and the search for them in acute cases, will cause them to elude discovery less and less frequently. The marked symptoms are pain and tumor.

Pain is almost never absent. It is epigastric, or in the right hypochondrium, and is very often referred directly to the seat of the gall-bladder. It may be so severe that the patient shrieks, especially when he moves (as in Budd's case), or rolls in agony (Barthez and Rilliet's case). It often occurs in severe paroxysms. In the great majority of instances it is associated with marked tenderness, which, however, is not apt to remain confined to the region of the gall-bladder, but to be found also over the whole of the right hypochondrium or right side of the abdomen; and the entire abdomen even may be sensitive, most likely then from a spreading peritonitis. On the other hand, the general tenderness may become localized in the region of the gall-bladder. In a few instances sensitiveness, without pain, is spoken of; in a very few, as in a case of Louis', pain is mentioned as absent. Rigidity of the abdominal walls, especially on the right side, not infrequently coexists.

Tumor is of diagnostic significance as great as or even greater than pain, though it is not so common a symptom. It is specially mentioned in 21 out of 53 cases, only, therefore, in less than one-half. But it is probably present in larger proportion; the typhoid state of the patient and the marked meteorism that generally exists prevent its detection. It occupies the seat of the gall-bladder, and is thus to be looked for at Mayo Robson's[1] point, namely, at the junction of the upper two-thirds with the lower third of a line drawn from the ninth rib to the umbilicus. In a number of instances it is described as pear-shaped and firm, also as being tender on pressure; it may be a mere resisting mass below the costal margin. The tumor of the gall-bladder may be noticed to disappear slowly, or, where perforation happens, the disappearance may be sudden. In some instances the tumor swells up from time to time, as in the remarkable case of Leudet,[2] in which a woman who left the hospital apparently well, though with signs of a tumor from typhoid cholecystitis still perceptible under the false ribs, had markedly recurring swelling with tenderness at each menstrual period for six months. The tumor that is found, though having its origin in the lesion in the gall-bladder, may not be due to this viscus strictly speaking, but, in the perforated cases, be a pus-

[1] Diseases of the Gall-bladder and Bile-ducts, 1897, p. 37.
[2] Clinique Médicale de l'Hôtel Dieu de Rouen, 1874.

cavity formed around it. The history of the case and the irregular shape of the swelling may lead us to suspect its cause, but there is no certainty in the discrimination.

Among the less marked symptoms are jaundice, nausea and vomiting, and chills. *Jaundice* occurred in 17 out of 58 cases, was thus absent or not mentioned in 41, and only occurs, therefore, in less than one-third of the cases. It is not, as a rule, deep, though, after it shows itself, it persists. It does not occur in the cases with perforation in any greater proportion; 5 only out of the 23 cases of perforation had jaundice. Nor is it of much more frequency in the suppurative cases, the proportion being 6 out of 24. Indeed, its relation to the gall-bladder lesions in typhoid fever is uncertain and of little value in diagnosis. In rare instances the jaundice is due to impaction of a gallstone, as in the case of Barbe,[1] in which attacks of gallstone colic and steadily deepening chronic jaundice preceded typhoid fever; and, at the autopsy, besides the characteristic intestinal lesions, a perforated gall-bladder was found and an obstruction of the common choledoch duct by a stone.

Nausea and *vomiting* occur as transient symptoms, though in much greater frequency than in the ordinary course of typhoid fever. They are mostly to be noticed at the beginning of the gall-bladder complication. In Legendre's[2] case the vomiting of large quantities of green, bitter fluid is specially mentioned. *Chills* are conspicuously absent. I find their occurrence noted in only 3 out of 54 cases, including the cases in which perforation happened. Burger's[3] case began with a severe chill; chills happened six days before death in Budd's[4] case, and happened also in one of Osler's cases. The other symptoms are those of severe cases of typhoid fever. But the frequent occurrence of pulmonary complications, especially toward the end of the fatal cases, is noteworthy. In a number of instances pneumonia was the immediate cause of death.

As regards the diagnosis of typhoid cholecystitis, this is impossible with any certainty, except where tumor is present, though it may be suspected if there be nausea and vomiting, a sense of weight, and sensitiveness over the gall-bladder. But the occurrence of tumor and of pain and tenderness at or near the seat of the gall-bladder make the diagnosis not difficult. The most likely error is confounding the malady with an appendicitis. As a rule, the seat of pain and tenderness and swelling is different; in the one case in the right iliac fossa, in the other in the region of the gall-bladder. But we cannot trust implicitly to this; as in appendicitis, especially at its upper part, or

[1] La France Méd., 1884, ii. p. 1071.
[2] Bull. de la Société Anatom. de Paris, 1881, p. 1893.
[3] Deutsch Arch. f. k. Med., 1873, p. 623. [4] On Diseases of the Liver, 3d ed., 1857, p. 196.

where the appendix is not normally situated, the localization of the symptoms may be high up; and in cholecystitis the pain and tenderness may not be most marked over the gall-bladder, and the swelling may be very difficult to define.

An exact discrimination of the different forms of typhoid cholecystitis cannot be always made. They are all most likely to come on late in the disease, or after convalescence has been established, and all, whether with or without perforation, as Hagenmüller[1] has clearly established, are prone to be associated with local peritonitis in the neighborhood of the gall-bladder. Where there are abscesses in other parts of the body, and we can exclude pylephlebitis and hepatic abscess, a *suppurative cholecystitis* may be inferred, if pain and tumor be present. If there be a history of biliary colic and gallstone, or if this arise in the progress of typhoid fever or not long subsequent to it, signs of cholecystitis mean suppurative cholecystitis. I think, too, though there are not many observations on this point, that examinations of the blood will help us materially. We know through the researches of Thayer[2] that in typhoid fever the number of white blood-corpuscles varies but little from the normal standard, about 6000 per c.cm. Marked leucocytosis, if there be symptoms of cholecystitis, points to its being suppurative, as in Mason's case and in Anderson's case, where there was perforation. On the other hand, in a case of Osler's that recovered, there was no leucocytosis, and we may infer the cholecystitis not to have been purulent. In laying stress on leucocytosis we must, however, exclude abscess of the liver, in which condition it may also exist. Yet here the local symptoms are different: there is less pain, no tumor over the gall-bladder, and in doubtful cases I should attach much importance to the occurrence of chills. The analysis in this paper has proved their extreme rarity in cholecystitis of any form, whereas they are very common in abscess and in pylephlebitis, as is sweating. In none of these conditions can we lay much stress on the presence or absence of jaundice. There are cases of gall-bladder affection in typhoid fever in which there is mere distention with bile or a watery fluid. Case IV. of this paper probably belongs to these. They have been supposed, as in the case of Dumoulin,[3] to be due to retention of bile owing to nervous disturbance attending the fever, analogous to the retention of urine; or they may be the result of obliteration of the cystic duct, as in a case of Louis,[4] where the bile in the distended gall-bladder had the appearance of urine, and the cystic duct was compressed by an enlarged lymphatic gland that surrounded it. No means exist of distinguishing these cases during life from acute cholecystitis, except it be by the absence of severe pain and

[1] De la Cholecystite dans la Fièvre typhoïde. Thèses de Paris, 1876, No. 269.
[2] Johns Hopkins Hospital Reports, vol. iv.
[3] Gaz. Méd. de Paris, 1848, p. 551.
[4] Fièvre Typhoïde, vol. i. p. 201.

very marked tenderness. Then it is likely that they are really instances of bacillary infection of the gall-bladder, and that the typhoid bacilli will be found in the fluid, only marked inflammation has not been induced.

Perforation of the gall-bladder has as its chief symptoms suddenly developed or intensified pain, collapse, and peritonitis. In some instances that have been reported there is also marked drop of temperature, as in the cases of Bonamy[1] and of Bond.[2] The effect on the tumor is often a decided lessening or a disappearance. Peritonitis, which may remain local, as in the case of Hawkins[3] and others, develops, and may lead to encapsulation of the discharged contents of the gall-bladder. On the other hand, a subsequent general peritonitis may occur. The course is often a comparatively slow one, two of the reported cases, Ranvier's[4] and Archambault's,[5] not dying until the twelfth day after the perforation.

It is evident how very similar the symptoms are to those of intestinal perforation. Gall-bladder perforation can be, indeed, distinguished only by the seat of the pain and the previous existence of the tumor. Should jaundice be present it would be an additional aid in discrimination. On the other hand, intestinal hemorrhages preceding the symptoms of perforation, and rapidly developing general peritonitis, belong more strictly to the intestinal lesion; local peritonitis in the upper part of the abdomen on the right side is more characteristic of gall-bladder perforation, as is a slower progress of the symptoms. Fall of temperature, too, attending the collapse, occurs much oftener in intestinal perforation in typhoid fever than in gall-bladder perforation in the same disease.

The *treatment* of the jaundice attending these different hepatic affections will be guided by our recognition of the probable cause. Those which are due to blood infection and to the finer parenchymatous changes in the liver cannot be reached by any special treatment, which must be that of the grave underlying typhoid condition. I will, however, point out that two of my cases recovered while taking decided doses of mineral acids, and this was also the result in two of Murchison's cases. In abscess of the liver, as well as in pylephlebitis, large doses of quinine may be employed. In the ordinary form of cholecystitis, recovery has followed applications of leeches over the swelling, followed by poultices, as in Observation No. LXVIII. of Frerichs. Besides the general treatment of the typhoid state, attention must be paid to the character of the discharges from the bowels; when very dark and showing vitiated bile, small doses of mercurials should be given. Leudet's[6] case got well under calomel and under frictions with belladonna.

[1] Gaz. Méd. de Nantes, 1890, p. 133.
[2] British Med. Journ., July 12, 1884, p. 67.
[3] Medico-Chir. Trans., vol. lxxx. p. 138.
[4] Bull. de la Soc. Anat., 1864, p. 433.
[5] Bull. de la Soc. Anat., 1852, p. 90.
[6] Loc. cit.

The suppurative cases require support, and, as soon as we are reasonably sure of their character, surgical interference, the admirable outcome of which was seen in the cases of Caspersohn,[1] of Williams and Shield,[2] of Alexieef,[3] of Mason,[4] of Osler and Halsted,[5] of Mark and Maurice H. Richardson.[6] Among the perforation cases I know of only one recovery without operation, the case of Salzman,[7] which discharged through the abdominal wall. An operation alone promises success, and how well it may succeed is proved by the results of Williams and Shield and one of the cases of Osler and Halsted.

THE SIGNIFICANCE OF ALBUMOSURIA IN MEDICAL PRACTICE; SUGGESTED BY A FATAL CASE OF ALBUMOSURIC MYXŒDEMA TREATED WITH THYROID EXTRACT.[8]

By Reginald H. Fitz, M.D.,
of Boston.

The following case of myxœdema is reported more particularly for the purpose of calling especial attention to the presence of a symptom which, with but a single exception, so far as I am aware, has hitherto been unrecorded in this disease except as a mere statement of fact in the *Practice of Medicine*, by Wood and Fitz. The patient therein referred to was seen by me in consultation with Dr. M. L. Chamberlain, of Boston, to whom I am indebted for permission to give the following account and for information concerning the progress of the malady.

The case is of further interest, if not importance, in showing that the prognosis of myxœdema still may be grave despite the immediate and repeated benefit so generally resulting from the use of thyroid preparations.

I first saw Mrs. — November 17, 1895. She was fifty-three years of age, and had lived the greater part of her life in Vermont. The last two years had been spent in California. She never had been pregnant.

As a girl she suffered considerably from discomfort referred to the stomach, in the region of which there would be a sense of distention for a day or two at a time. Cramps would occur suddenly, and tenderness along the spine was complained of. With these exceptions she en-

[1] Festschr. f. Fr. von Esmarch, 1893, p. 455, Kiel and Leipzig. [2] Lancet, March 2, 1896.
[3] Journ. Dietskaya Med., 1896, No. 4. Quoted in The American Journal of the Medical Sciences, Oct., 1897, p. 466.
[4] Trans. Assoc. American Physicians, 1897. [5] Ibid.
[6] Boston Med. and Surg. Journ., December, 1897.
[7] Med. Corresp. Würtemb. Arztl. Verein., 1870, xl. 84.
[8] Read at the annual meeting of the Association of American Physicians, Washington, D. C., May 3, 1898.

joyed good health throughout the greater part of her life, recalling to mind solely an operation for anal fistula when she was about forty-seven years old.

At the age of forty-nine, while in Vermont, she observed a gradual loss of flesh, strength, and color. A year later, when tired, would feel a griping sensation in the back of the neck and a pain between the shoulders. These discomforts were noticeable especially on going down hill. There was also a temporary stiffness of the joints in the morning. At this time the eyelids were slightly swollen and an increased flow of saliva began, a symptom which has continued since, and persists at present.

In the following year, 1893, while in California, the joints again became appreciably stiff, and she felt a sense of numbness in the right heel, in the knees immediately above and below the joint, and in the fingers of the right hand. In 1894 the stiffness diminished somewhat, but the numbness persisted. In the fall of this year the teeth were troublesome and, despite the care of a dentist, became painful, and since have remained in this state. An upper canine tooth is said to have extended into the bone one-fourth of an inch. There was a metallic taste in the mouth, and she became unable to masticate resistant food, being obliged to live upon soft articles of diet. Walking now caused so much fatigue that she was obliged to give up active exercise. The griping at the back of the neck and the pain between the shoulders continued to be annoying at times, and she suffered also from wakefulness.

In January, 1895, superficial swellings first were noticed. They appeared as an enlargement of the back of the neck, a lump beneath the jaw, hypertrophy of the tongue, and, later, indurations in the legs and arms. At first the swellings would vary temporarily in size, and that in the neck would lessen somewhat under the influence of fomentations; but later the enlargement remained constant. The voice was now changed, and the increased flow of saliva became a more or less constant drooling. In the course of a few months, in consequence of a loose molar tooth, the jaws were prevented from closing. The tooth was extracted, but the jaw and the neighboring portion of the tongue became sore and, finally, a fragment of dead bone was removed.

At the time of my first visit Mrs. — was unable to walk, on account of muscular stiffness. There was no evidence of mental impairment, nor had such been observed by her friends. Her face was pale, moderately swollen, and expressionless from partial effacement of wrinkles and furrows. In sharp contrast was the elevation of the eyebrows and wrinkling of the forehead from apparent tension of the occipito-frontalis muscle. The upper eyelids were relatively normal, but the lower lids were somewhat puffy. The lips were slightly thickened and everted, the surface roughened. Especially conspicuous was the greatly enlarged and resistant tongue, filling the partially opened mouth. The dorsum of the tongue was dry, although the flow of saliva was constant. The submaxillary region was prominent, presenting the appearance of a double chin, and both submaxillary salivary glands were greatly swollen and dense. The back of the neck was smooth and much swollen, like that of a very obese person, but was dense and resistant to the touch. It measured from sixteen and one-half to seventeen and one-half inches in circumference. The hands and feet were cold. The skin covering the back of the hands was thickened, coarsely wrinkled, the surface being rough and of a dirty-

yellowish tint, the whole appearance suggesting that of a fowl's claw. The skin covering the front of the chest and abdomen was normal, but that of the forearms, legs, feet, back, and buttocks was pale, dry, smooth, tightly drawn, not displaceable from the subjacent structure in consequence of the resistance of the subcutaneous tissue. The anterior wall of the vagina was smooth, thickened, and dense like the abnormal portion of the skin. There were no supraclavicular swellings. The hair was coarse and dry, but the nails were normal in appearance. The thyroid gland was not palpable. Nothing abnormal was found on auscultation and percussion of the chest and on palpation of the abdomen. The temperature was 98.4° F. The examination of the blood by Dr. R. C. Cabot showed 5,030,000 red corpuscles, 11,600 leucocytes, and 35 per cent. of hæmoglobin. The differential count gave 74 per cent. of polynuclear leucocytes and 23 per cent. of lymphocytes.

On the addition of nitric acid to the urine a dense, white precipitate was formed, occupying nearly one-half the volume of urine. The precipitate was dissolved when the specimen was boiled, but reappeared on cooling. When the urine in a test-tube was boiled it became opaque until the boiling-point was reached. It then became clear, and thus remained until the liquid was cool, when a white precipitate formed. Under the microscope a few red blood-corpuscles and an occasional hyaline and granular cast were seen.

The dissolving of the nitric acid precipitate by heat and the formation of a white precipitate when the boiled urine was cooled led me to suspect the presence of albumose, and Prof. E. S. Wood was asked to test further for this substance. He informed me that after boiling and filtering the urine to free it from albumin the clear filtrate, when acidulated with acetic acid and heated gently, became opaque, but the opacity disappeared on boiling, and a white precipitate formed when the fluid was cooled. Acetic acid and ferrocyanide of potassium gave a precipitate which dissolved when the mixture was boiled, and reappeared as the temperature fell. The biuret reaction was positive.

Professor Wood analyzed the urine from this patient repeatedly during a period of six weeks. A trace of albumin was present usually, but albumose was found constantly, by estimate varying from $\frac{1}{8}$ per cent. to $\frac{1}{4}$ per cent. December 10, 1895, a quantitative determination was made and showed 0.93 per cent. of albumose. The per cent. of urea on this day was 3.63, and the total quantity 18.66 grammes.

The diagnosis of myxœdema was made, and the treatment with thyroid extract begun, the five-grain tabloids of Burroughs, Wellcome & Co. being used. The dose of five grains on the first day was increased by one tabloid daily, but on the third day there was a sense of præcordial oppression, and the pulse became quickened. The dose then was diminished to one or two tabloids daily for a week, when it again was raised to three five-grain tabloids in each twenty-four hours.

I saw Mrs. — a second time December 10, 1895, a little more than three weeks after my first visit. The change in her appearance had greatly improved, although previous to the use of the thyroid extract her condition was steadily deteriorating. At the end of the first week of thyroid treatment the œdema suddenly left the eyelids, but a watery œdema, pitting on pressure, appeared and persisted in the feet. The flow of saliva diminished, the swollen tongue became smaller, and the

pain in the shoulders was less disturbing. In the third week of treatment the swelling of the neck and of the submaxillary glands was noticeably lessened, and the expression of the face became more mobile. The weight at the beginning of the thyroid treatment was one hundred and twenty-five and one-half pounds, and there had been a loss of about three pounds each week. The quantity of urea eliminated increased from eleven to sixteen grammes. The appetite was unaffected, but the pallor and debility were greater than when first seen. The pulse varied between 83 and 107 beats per minute, and the temperature remained in the vicinity of 99.7° F.

It was considered desirable to continue the use of the thyroid extract under careful supervision, that cardiac weakness might not prove a source of danger. The especial discomforts produced by it were fleeting pains in the muscles or in one joint or another, præcordial constriction, and a choking sensation, all more likely to occur at night when the greatest quantity of the thyroid preparation had been taken within a limited number of hours.

Preparations of iron, arsenic, manganese, strychnine, digitalis, and nitroglycerin were given from time to time as the indications for their use were apparent. On account of the progressive weakness of the patient, despite the early improvement in the surface manifestations, the thyroid preparations were discontinued from time to time.

At a third visit, February 25, 1896, Dr. C. F. Folsom also saw the patient. At this time, although the expression was brighter, she was pale, weak, and emaciated. The especial improvement was in the condition of the skin, which was smooth, moist, and free from the yellow discoloration so marked at the outset. The hands were warm, the hair was moist and less bristling, but the brawny induration of the back of the neck and the swelling of the tongue and submaxillary glands had not materially diminished in the previous two months. It was decided to continue the use of the thyroid, and from seven to nine grains were daily given for a week, during which time the pulse was about 100 and the temperature varied from 99.3° to 100.4° F. A sudden severe attack of præcordial pain then occurred, and the use of the thyroid was discontinued for four weeks. During this time the pulse fell to the normal and became stronger, the salivation lessened, the weight increased somewhat, but the tongue felt as if it was somewhat enlarged. The thyroid extract was then given in one-grain doses, and, for greater convenience in supervision and care, Mrs. — entered the Boston City Hospital, where she came under the charge of Dr. Folsom, to whom I am indebted for the report of her further progress.

She was admitted to the hospital April 18, 1896. The circumference of the neck then was fifteen inches, the tongue was about four inches wide and one inch thick. The head could not be bent backward, nor could the chest be touched with the chin. The hands and feet were cold, the skin was smooth, and the hair moist. The blood examination showed 84 per cent. hæmoglobin, 4,532,000 red corpuscles, and 10,500 leucocytes. The patient received one grain of thyroid extract daily, but she gradually became weaker, took little nourishment, decidedly failed on April 26, and died early on the following day. There was no autopsy.

There having been some difference of opinion among the physicians who saw this patient as to the exact nature of the disease, the reasons

for the diagnosis of myxœdema may be summarized. There were present "the firm swelling of the skin, not pitting on pressure, inelastic, adherent to the parts beneath, and not affected by gravitation; the dryness and roughness of the skin, tending, with the swelling, to obliterate all lines of expression; the imperfect nutrition of the hairs . . the local tumefaction of the skin and subcutaneous tissue noticed in various parts of the body . . an affection of the teeth homologous with that of the hairs just mentioned; the remarkable physiognomy; the slow . . monotonous voice . . and elimination or apparent absence of the thyroid gland." These are among the characteristics of myxœdema described in the *Report of the Committee of the Clinical Society of London*, 1888 vol. xxi., Supplement, p. 178. The mental impairment and subnormal temperature alone are lacking to complete the picture. But mental disturbances were absent in twenty-seven out of forty-six cases tabulated by the committee.[1] The temperature was normal in eight cases, and in a few was 99.6 F., or even higher, though never above 100° F. The swelling in the back of the neck was duplicated in Dr. Ord's case, No. 87, in which there was a "swelling at the back of the neck over trapezius, so that he cannot bear to wear a collar." Salivation was present in three of the committee's cases, and the submaxillary gland of Hale White's cases[2] showed marked changes. A large, swollen tongue was noted in fifty-two cases.

If the correspondence in clinical characteristics is not considered as sufficient for the confirmation of the diagnosis, additional evidence is furnished by the effects of the treatment with the thyroid extract. According to Murray[3] there are rise in temperature, disappearance of swelling, loss of weight, a soft, smooth, most condition of the skin, growth of the hair, improvement in the mental condition, and increase in the elimination of urea. Her temperature became somewhat higher, and the previously cold hands were warm. The swelling diminished, there was a loss of weight, the skin became soft, smooth, and moist, and the elimination of the urea increased. A growth of hair was not conspicuous, since there was no tendency to alopecia, but a considerable improvement in its nutrition was apparent from the return of its normal characteristics.

The failure of the thyroid treatment to accomplish more marked relief is in striking contrast to the almost constant benefit derived from its use in the treatment of myxœdema. Mitchell Clarke,[4] however, reports two cases in which thyroid treatment proved unsuccessful, and Macpherson,[5] although causing improvement by thyroid grafting, did

[1] Report of the Committee of the Clinical Society of London, 1888, vol. xxi., Supplement, p. 14.
[2] Op. cit., p. 41.
[3] Twentieth Century Practice, 1895, vol. iv. p. 712.
[4] British Medical Journal, 1892, vol. ii. p. 451.
[5] Edinburgh Medical Journal, 1892, vol. xxxvii. p. 1021.

not remove the myxœdematous condition. Byron Bramwell[1] gives an account of two fatal cases of myxœdema during or shortly after thyroid treatment. In each instance the death was sudden.

I am indebted to my colleague, Dr. E. G. Cutler, for the following summary of a fatal case under his charge.

"A patient in whom I made the clinical diagnosis of myxœdema had gradually over a period of a year and a half come into the following condition: The skin of the face, neck, shoulders, hands, arms, legs, and feet was pale and a little glossy, rather dry, much distended by a subcutaneous growth which did not pit and apparently was not fat. The wrinkles in the face were obliterated, the hair on the head had become sparse and dry, the hands and feet were much wrinkled, and the skin and nails coarse and rough. Speech was slow and peculiar. The mental condition was variable: at times the patient was rather inclined to be talkative, but the range of subjects was limited; at other times the patient would be quiet for hours and rather somnolent. Frequently there was mild delirium at night, with occasional hallucinations of sight. The patellar reflex was absent. The pulse was slow, the surface cool, and the temperature in the mouth 98° F., though no complaint of cold was made. The urine was free from albumin. The thyroid could not be made out. Toward the end there was marked tendency to somnolence. Thyroid tablets, five grains each, were given up to nine a day for two months, beginning with small dose, but with little effect. Death was sudden and apparently due to syncope."

The novel feature of my case was the albumosuria, which continued throughout the progress of the disease from the time it first was observed. Occasional or slight traces of albumin were noticed in twenty out of ninety cases, and in one a large quantity, in the series tabulated by the London Clinical Society's Committee,[2] in which mention was made of this condition, and in twenty-one out of one hundred and twelve cases collected by Hun and Prudden.[3] Murray[4] states that "mucin" has not been found in the urine of human myxœdema, but refers[5] to Halliburton's discovery of an abundance of "mucin" in the urine of a sheep that developed myxœdema two years after the thyroid was removed by Horsley. Buzdyan,[6] however, found traces of mucin, but no albumin, in the urine of a patient examined by him. The only instance of myxœdema in which I have found mention of the occurrence of albumosuria is the patient of von Jaksch.[7] The case was one of typical Basedow's disease in which there were present a swelling of the legs, regarded as myxœdematous, and an albumosuria observed during a period of six months.

As is well known, this term is applied to the presence in the urine

[1] Edinburgh Hosp. Rep., 1895, vol. iii. p. 116.
[2] Op. cit., p. 21.
[3] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1888, vol. xcvii. p. 1.
[4] Loc. cit., p. 722.
[5] Loc. cit., p. 726.
[6] Wien. klin. Wochenschr., 1891, Band iv. p. 510.
[7] Prag. med. Wochenschr., 1892, Band xvii. p. 602.

of a peculiar substance first observed by Bence Jones[1] in 1845. As described by him, "It gave no precipitate with an excess of nitric acid unless left to stand, or unless heated and left to cool, when it became solid. This solid redissolved by heat and again formed on cooling. Continued boiling with strong nitric acid evolved but little gas, and did not quickly hinder this reaction. Hydrochloric acid gave the same solid precipitate, soluble by heat. Strong acetic acid gave only a slight precipitate, which redissolved by heat. Caustic potash and sulphate of copper gave a splendid bright-blue, clear liquid, passing over, when heated, to a claret color, . . coagulated firmly with heat, very perfectly with a drop or two of acetic acid."

According to Maly[2] the product of the gastric digestion of albuminous substances was designated albuminose by Mialhe in 1846, but subsequently Lehmann named it peptone. Meissner and his pupils, in a series of articles published between 1847 and 1853, assumed the existence of a number of products of digestion intermediate between albumin and peptone, to which the terms parapeptone, metapeptone, dyspeptone, α, β, and γ peptone were applied. In 1869 Kühne received from Stokvis a specimen of urine which presented reactions similar to those observed by Bence Jones, and Kühne regarded the substances as identical. In the same year Gerhardt[3] sought in the urine for other albuminous substances than serum albumin, and discovered a variety, called by him "latent," which resembled in its characteristics one of the peptones described by Meissner. He found it in a number of diseases, and observed that it was to be met with in persons whose temperature, frequently or constantly, was in the vicinity of 104° F. Senator[4] later observed in the urine easily distinguishable quantities of what he regarded as peptone. He recognized that this substance might have been produced in albuminous urine by the process of boiling used in its isolation, but suggested that it may have been present in the freshly voided urine. In support of this view he referred to Gerhardt's discovery of a substance resembling peptone in urine in which no evidence of ordinary albumin was to be obtained. Leick,[5] however, states that, although boiling may produce albumose from albumin, such a result does not necessarily follow, since numerous specimens of albuminous urine were so treated without the formation of albumose. Even in experiments on isolated albumin the quantity so transformed was too small to be significant. It was recognized also by Senator as possible for the albumin or albuminous urine, on its passage from the kidneys to the bladder and during its retention in this viscus, in part to be con-

[1] Philosoph. Trans. Royal Soc. London, 1848, Pt. i. p. 55.
[2] Herrman's Handb. d. Physiol., 1881, Band v. S. 94.
[3] Deutsches Arch. f. klin. Med., 1869, Band v. S. 212.
[4] Arch. f. path. Anat., etc., 1874, Band lx. S. 476.
[5] Deutsche med. Wochenschr., 1896, Band xxii. S. 22.

verted into peptone, in accordance with the statement of Eichwald, that fluid albumin in contact with animal tissues at the temperature of the body is readily transformed into peptone. Eichwald found this substance in the urine of nephritis, and Obermüller, in 1873, in that of scarlet fever and Asiatic cholera. Gowers[1] a few years later noticed its presence in a patient who previously had suffered from glycosuria.

About this time Kühne gave the term hemialbumose to this substance, which was considered to correspond with the *a*-peptone of Meissner, and Schmidt-Mülheim[2] designated it propeptone. Its properties were studied also by Salkowski.[3] All these observers recognized the resemblance between this so-called peptone, hemialbumose, or propeptone, and the substance discovered by Bence Jones. The methods employed for the recognition of the "peptone" were faulty, especially from the difficulty of wholly removing the albumin often associated, and from the frequent, if not constant, presence of "mucin," which also was precipitated by the alcohol used in isolating the substance, and which gave rise to reactions similar to those attributed to the peptone. Hofmeister[4] consequently devised a method for the isolation of the so-called peptone which should free it from these sources of error. This method and the improvement subsequently made by Salkowski served as the basis of numerous contributions to the study of what has been designated "peptonuria."

The researches of Kühne and of Kühne and Chittenden[5] led to the use of the term albumosuria as a substitute for propeptonuria. According to these investigators albumose, hemialbumose, or propeptone was a mixture of four albumoses which were designated protalbumose, deuteroalbumose, heteroalbumose, and dysalbumose. Each varied slightly from the others, especially with reference to the degree of solubility in water and in behavior toward solutions of sodium chloride, being either soluble or insoluble in dilute solutions and precipitated by concentrated solutions alone or in the presence of an acid according to the variety of albumose concerned. When in solution they were not precipitated by heat alone, but if precipitated by acids or salts were redissolved at a boiling temperature and were precipitated when the solution was cooled. According to Huppert, Mathes, and Rosin they become opaque at temperatures of 150°–152° F., and clot at 166°–178° F. They were precipitated by nitric acid and by acetic acid, by magnesium sulphate, concentrated solutions of sodium chloride, and of ammonium sulphate in an acid, alkaline, or neutral solution, and gave the biuret reaction.

[1] Lancet, 1878, vol. ii. p. 3.
[2] Arch. f. Physiol., 1880, S. 33.
[3] Arch. f. path. Anat., 1880, Band lxxxi. S. 552.
[4] Ztschr. f. Physiol. Chem., 1880, Band iv. S. 253.
[5] Ztschr. f. Biol., 1883, Band xix. S. 159, 219; 1884, Band xx. S. 11.

Like albumin, they were precipitated by nitric acid, ferrocyanide of potassium and acetic acid, sodium chloride and acetic acid, and ammonium sulphate, but they were not coagulated on boiling. They resembled peptones in being soluble at a boiling temperature, precipitating as the fluid became cool, and in giving the biuret reaction. They differed from peptone, according to Kühne,[1] in being precipitated by ammonium sulphate.

The search for albumose then became instituted, and the term albumosuria soon replaced that of propeptonuria, although for a long time it was considered to be a different condition from peptonuria.

The distinction made between albumoses and peptones, based upon the insolubility of the former in ammonium sulphate, was opposed by the observation of Neumeister[2] that this agent does not precipitate entirely all the albumoses, especially deuteroalbumose. Stadelmann in 1894 concluded that peptone as distinguished from albumose never occurred in fresh urine, although it might be found in stale albuminous urine from the action of bacteria upon the albumin. Von Noorden and Senator[3] accepted this view, and maintained that both peptonuria and propeptonuria were albumosuria. According to Senator, if a part of the urine which gives a positive reaction to Salkowski's test, and, therefore, is considered to contain peptone, is slightly acidified and treated with ammonium sulphate in excess and filtered, there will be no biuret reaction in the filtrate, indicating the absence of Kühne's peptone, which should be soluble in the ammonium sulphate.

Albumose was found not only in the gastric contents during the digestion of albumin, but also in artificial peptone preparations and by Fleischer[4] in normal bone-marrow. The discovery of its presence in semen is generally attributed to Posner,[5] but this observer and others who have written upon the subject, with the exception of Kahler,[6] have overlooked the fact that Bence Jones,[7] the discoverer of albumose, found it not only in the urine and in pus, but also "in the secretion from the vesiculæ seminales." Virchow[8] recognized in the bone-marrow of osteomalacia a substance which he considered to resemble that described by Bence Jones. Salkowski[9] sought successfully for it in the liver and spleen of leukæmia and in the liver of acute yellow atrophy. Miura[10] observed it in the liver, heart, and kidneys of phosphorus poisoning produced experimentally, and in the organs of a case of puerperal

[1] See article by Wenz: Ztschr. f. Biol., 1886, Band xxii. S. 1.
[2] Ztschr. f. Biol., 1888, Band xxiv. S. 267.
[3] Deutsche med. Wochenschrift, 1895, Band xxi. S. 217.
[4] Arch. f. path. Anat., etc., 1880, Band lxxx. S. 482.
[5] Berlin. klin. Wochenschrift, Band xxv. S. 417.
[6] Prag. med. Wochenschrift, 1889, Band xiv. S. 33.
[7] Arch. f. path. Anat., etc., 1852, Band iv. S. 309.
[8] Loc. cit.
[9] Loc. cit., 1880, Band lxxxi. S. 166; 1882, Band lxxxviii. S. 394.
[10] Loc. cit., 1885, Band ci. S. 316.

fever. Schültzen and Riess[1] previously had found albumose in the urine of phosphorus poisoning. Fischel[2] stated that albumosuria was present almost constantly during the involution of the puerperal uterus, and Kottnitz[3] when there was a macerated fœtus.

Albumosuria has been produced experimentally by Lassar[4] by rubbing petroleum into the skin of animals. Plosz and Gyergai[5] and Hofmeister[6] caused it by the injection of peptone into the veins, and Jitta[7] by the subcutaneous injection of glycerin. Rosenheim[8] states that he has seen albumosuria follow the ingestion of large quantities of albumose in a case of severe intestinal disturbance.

The clinical importance of albumosuria has been made a matter of study by many observers whose results in the main agree. Although published under the titles of peptonuria, propeptonuria, or albumosuria, the method used for the purpose of determining the presence of the albumose was that of Hofmeister, or, in more recent years, by this method as modified by Salkowski.[9] The chief advantages of the modification are gain in time and the use of a much smaller quantity of urine.

The urine to be tested must first be freed from any albumin present by acidifying from 30 to 50 c.c. with acetic acid, adding an equal quantity of saturated solution of common salt, boiling, and filtering. The albumins and albumoses are precipitated, but the latter are redissolved at the boiling temperature. The filtered fluid containing the albumose in solution is to be placed with a few drops of hydrochloric acid in a beaker, and then a solution of phosphotungstic acid is to be added while precipitation continues. The precipitate is to be consolidated by gentle heat into a coherent or powdery substance. The supernatant fluid is to be poured off, and the precipitate, washed with water, is to be dissolved in a solution of soda (specific gravity 1.16), which is to be added drop by drop until a blue or a colorless solution results. The solution, if blue, is to be decolorized by heat, and a few drops of a 1 per cent. solution of sulphate of copper are to be added to the soda solution, when a red or violet color, the biuret reaction, results if albumose is present.

Recently Salkowski[10] has called attention to a possible source of error. He has found that urobilin, which is precipitated by phosphotungstic acid, gives also the biuret reaction, and that consequently a specimen

[1] Ann. d. Char-krankenh. zu Berlin, 1869, Band xv. S. 1.
[2] Arch. f. Gynäkol., 1884, Band xxiv. S. 400.
[3] Deutsche med. Wochenschrift, 1888, Band xiv. S. 613.
[4] Arch. f. path. Anat., etc., 1889, Band lxxvii. S. 157.
[5] Arch. f. d. ges. Physiol., 1875, Band x. S. 53.
[6] Zeitschr. f. physiol. Chem., Band v. S. 127.
[7] Jahresb. u. d. Fortschr. d. Thier. Chem., 1885, Band xv. S. 474.
[8] Allg. med. Centr., 1897, Band lxvi. S. 1132.
[9] Centralblatt f. d. med. Wissensch., 1894, Band xxii. S. 113.
[10] Berlin. klin. Wochenschrift, 1897, Band xxxiv. S. 353.

of urine tested by the Salkowski method may give a positive result, but due to urobilin and not to albumose. Urobilin in the urine does not necessarily produce this reaction, but is more likely to in case the spectroscopic examination of the urine gives a well-marked urobilin line. Leick[1] already had suggested a modification of the Salkowski test, having found it necessary to use a stronger soda solution or a larger quantity of the weaker variety. After removing the albumin he added also the neutral lead acetate to the filtrate for the purpose of precipitating "mucin," coloring matter, and any remaining albumin. According to Salkowski, albumose also is precipitated by this reagent, and the negative results of the examination by this method could not exclude the possibility of albumosuria. Fortunately for practical purposes, the question relates to quantity and not to mere presence. Bang[2] also has devised a method for finding albumose in the urine, even in a dilution of 1:4–5000, when urobilin is present in any considerable quantity. A test-tube containing 8 grammes of finely powdered ammonium sulphate in 10 c.c. of urine is to be heated till the former is dissolved. The contents are to be boiled for a minute, centrifuged for another minute, and the clear liquid poured off. The residue, containing albumose, albumin, urobilin, uric acid, and urates, is to be stirred in alcohol (97 per cent.), which dissolves the urobilin and is to be poured off. This residue is boiled with a little water and filtered; the filtrate gives the biuret reaction if albumose is present. The centrifuge may be dispensed with, if the quantity of albumose is considerable, and the following method employed. After boiling some of the albumose adheres to the wall of the tube. The liquid is to be poured out and the adherent residue washed with alcohol to which a little chloroform is to be added if there is presumably much urobilin. The biuret test is to be applied to the filtrate from the residue dissolved in water. The presence of urobilin in the alcoholic extract is shown by a fluorescence when a few drops of a solution of zinc chloride are added. Hæmatoporphyrin may simulate albumose by causing a red color when the alkali of the biuret test is used. Its presence is to be suspected if the alcoholic extract is red and proven by the spectroscope. If, therefore, the alcoholic extract is red the urine should first be treated with barium chloride, which precipitates hæmatoporphyrin.

Maixner,[3] von Jaksch,[4] and Pacanowski[5] examined hundreds of cases of various diseases by Hofmeister's method, and came practically to the same conclusion, that albumosuria was oftenest found in suppurative processes associated with the retention and disintegration of pus,

[1] Loc. cit.
[2] Deutsche med. Wochenschrift, 1898, Band xxiv. S. 17.
[3] Vrtljschr. f. d. prakt. Heilk. Prag., 1879, Band cxliv. S. 75; Ztschr. f. klin. Med., 1881, Band viii. S. 234.
[4] Zeitschr. f. klin. Med., 1883, Band vi. S. 413.
[5] Ibid., 1885, Band ix. S. 429.

in acute infectious diseases, and in affections with more or less extensive destruction of tissues. Köppen[1] observed it in a number of insane persons, especially those who were maniacal or delirious. W. Robitschek,[2] Senator,[3] and Leick,[4] using Salkowki's method, arrived at a similar result. The albumosuria was relatively constant in deep-seated suppuration and in acute fibrinous pneumonia, especially during resolution.

Gerhardt's claim that ordinary or "latent" albuminuria occurred in persistent or frequent elevations of temperature above 104° F., and the statement of Krehl and Matthes[5] that albumosuria was almost constant in fever, are subject to a different interpretation in the light of Salkowski's discovery concerning the reaction of urobilin.

Albumosuria has been found in various chronic affections, as well as in those of an acute nature. Among these chief importance is to be attached to the albumosuria of osteomalacia or of affections regarded as of this nature.

Such cases have been reported by Bence Jones,[6] Kühne,[7] Kahler,[8] Stokvis and Ribbink, Matthes,[9] Huppert,[10] and Rosin.[11] According to Kahler, these are not examples of true osteomalacia, but of myelogenous tumors, sarcoma, lymphoma, myeloma, especially of the bones of the thorax. Matthes,[12] in four cases of osteomalacia which probably were of multiple myeloma, isolated from the urine a substance with the characteristics of albumose, but which, when digested for some time, gave rise to a ferrated nuclein. Hence the substance was regarded as a nucleo-albuminose arising from the ferrated nucleo-albumin of bone-marrow discovered by Nasse. It was not found in typical puerperal osteomalacia.

Raschkes,[13] on the contrary, states that albumosuria occurs in senile osteomalacia, and Hammer[14] and Marckwald[15] make no mention of the importance of albumosuria in their analyses of the reported cases of multiple sarcoma or of allied affections of the bones.

In most of the diseases in which albumosuria has been found the albumose has been observed, as a rule, for a short time and in small quantity, although in rare instances for a long time and in large quantities. Pacanowski,[16] indeed, subdivided the condition into acute and

[1] Arch. f. Psychiat., 1888-1889, Band xx. S. 825.
[2] Zeitschr. f. klin. Med., 1884, Band xxiv. S. 556.
[3] Deutsche med. Wochenschrift, 1895, Band xxi. S 217.
[4] Loc cit.
[5] Deutsches Archiv f. klin. Med., 1895, Band liv. S. 501.
[6] Loc. cit.
[7] Loc. cit.
[8] Prag. med. Wochenschrift, 1889, Band xiv. S. 35.
[9] Verhand. d. Cong. f. innere Med., 1896, Band xiv. S. 476.
[10] Zeitschr. f. physiol. Chem., 1896-97, Band xxii. S. 500.
[11] Berlin. klin. Wochenschrift, 1897, Band xxxiv. S. 48.
[12] Loc. cit.
[13] Prag. med. Wochenschrift, 1894, Band xix. S. 649.
[14] Archiv f. path. Anat., etc , 1894, Band cxxxvii. S. 280.
[15] Ibid., 1895, Band cxli. S. 128.
[16] Loc. cit.

chronic albumosuria. But his distinction applied solely to the occurrence of the symptoms in acute and in chronic affections. A more practical division is into transitory and persistent albumosuria. Transitory albumosuria is to be found, despite the faulty methods and the opportunities of error, in such a variety of diseases as to have proven of but little practical value except in the diagnosis of acute pneumonia, deep-seated suppuration, including meningitis, and of macerated fœtus. In all of these conditions the ordinary means of diagnosis are usually sufficient, and the leucocyte count affords a most satisfactory aid, and is an efficient substitute for the search for albumose.

Greater value is to be attached to the recognition of persistent albumosuria, the importance of which in practice has become especially suggested of late years in connection with the diagnosis of multiple but latent tumors of the trunk. Such an albumosuria is sometimes nearly a pure form, and is spoken of as primary or typical, better, perhaps, as persistent or excessive. This variety thus far has been observed principally in multiple bone tumors and in myxœdema, and in but few cases of these affections. These observations, however, are so suggestive as to demand general attention.

It has been my fortune in the past two years to have seen two cases of persistent and excessive albumosuria, so generally recognized as an exceedingly rare condition. The first case serves to introduce this communication; the second, now in charge of my colleague, Dr. F. C. Shattuck, to illustrate it. In the latter the presence of albumosuria, and its extreme degree, led to the probable diagnosis of multiple tumors of the bones, and the use of the Röntgen rays showed such changes in the structure of the bones as confirmed this opinion.

The source of the albumose in these cases may prove to be in the bone-marrow, as suspected by Virchow, but chemical analyses to determine this point have yet to be made. It is important also that the subcutaneous tissues in myxœdema should be examined chemically for albumose, since the nature of the infiltrating substance in this disease is still a matter of conjecture, and the presence of albumose in the urine of the two cases suggests a possibility requiring disproof, even if the search give no other information.

Whatever the value of albumosuria may be in diagnosis, its persistent and excessive presence is apparently a sign of grave prognosis, since the cases in which this condition has been found have, almost without exception, proven fatal.

INFECTIOUS MULTIPLE GANGRENE OF THE SKIN.[1]

By M. B. Hartzell, M.D.,
INSTRUCTOR IN DERMATOLOGY, UNIVERSITY OF PENNSYLVANIA; DERMATOLOGIST TO METHODIST EPISCOPAL HOSPITAL, PHILADELPHIA.

The recorded cases of multiple gangrene of the skin include two distinct varieties which differ considerably in their clinical features and are widely separated pathologically. Doutrelepont, Kaposi, Renaut, Bayet, Duhring, and others have reported cases under various names, occurring for the most part in nervous or hysterical women, which were, without doubt, trophoneurotic in nature. In these the cutaneous lesions were usually flaccid vesicles or bullæ, less frequently pustules, occurring in some instances in more or less well-defined groups, followed in a short time by gangrene of the skin, as a rule, superficial in extent, but in exceptional cases causing extensive losses of tissue. The course of the disease was commonly irregular, now better, now worse, lasting from a few months to several years. In a much smaller number of cases an infectious origin has been demonstrated by the finding of special micro-organisms in the lesions which culture and inoculation experiments proved to be pathogenic; or their infectious nature has been reasonably inferred from their symptoms and course.

The following case presents a somewhat unusual type of infectious gangrene of the skin, being characterized by some clinical and bacteriological features not noted in those hitherto reported:

Mrs. H. B., aged forty-six years, the wife of a farmer; pale and somewhat emaciated; was first seen in August of this year, through the courtesy of Dr. Zook, of Newville, Pa., under whose care she had been for three or four years. At the time of this first examination there were present upon the arms and legs six or eight perfectly round, deeply excavated, sharply circumscribed ulcers, and innumerable very white, mostly circular, smooth, slightly depressed scars varying in size from a pea to a silver dollar. Upon the right shoulder over the deltoid muscle was an especially large ulcer, two and one-half or three inches in diameter and extending down to the superficial fascia, the large size of this lesion being due to the fact that it had been allowed to pursue its course without treatment of any kind for three or four weeks. Some of these ulcers presented healthy granulating surfaces; others were covered with grayish or black moist sloughs.

Five weeks later the patient again came under observation in the wards of the Methodist Hospital of this city, to which she had come for the further study and treatment of her malady. Upon her admission to the hospital there were present a number of lesions in various stages of development or involution, a few upon the trunk, but the majority upon the arms and legs. Upon the upper part of the chest were four circular,

[1] Read before the College of Physicians of Philadelphia, January 5, 1898.

thick, black crusts, beneath which were shallow, granulating ulcers about an inch in diameter. About the centre of the flexor surface of the left forearm was a pea-sized, oval, black eschar, surrounded by an elevated vesicular ring an eighth of an inch wide, about which was a dark-red

FIG. 1.

Infectious multiple gangrene of skin. Vacciniform lesion on left forearm, about one week old. Numerous scars from old lesions.

inflammatory areola, the whole bearing a close resemblance to vaccinia just before the contents of the vesicle become purulent. This lesion was the seat of considerable pain, and was very firm and tender to the touch (Fig. 1). On the inner surface of the left thigh, about six inches below Poupart's ligament, there were three circular ulcers an inch or more in

FIG. 2.

Infectious multiple gangrene of skin. Ulcerating lesions on inner surface of left thigh.

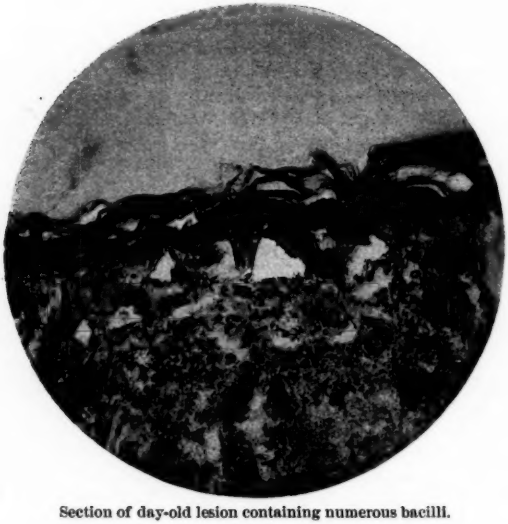
diameter, two of which were clean and granulating, while the third and largest was surrounded by an elevated border quite firm to the touch, on top of which was a flat, ill-defined, vesicular ring, the bottom being covered with a grayish, loosely adherent slough; this ulcer was also extremely painful (Fig. 2). Upon the left leg were several shallow

healthy ulcers which were rapidly healing; these had been the seat of gangrenous lesions which had been excised before the patient's admission to the hospital. As has already been mentioned, there were, in addition to these active lesions, numerous scars, the sites of former ones upon the chin, upper part of the chest, and upper and lower extremities. It is worth noting that the lower part of the chest, the abdomen, and the entire back were entirely free from evidences of disease past or present. The early history of the affection was briefly as follows: Four years ago the patient ran a meat-hook, which had been in use for some time, under the nail of the third finger of the right hand; shortly after this injury a painful spreading ulcer formed in this situation, which was followed by a second just above the right internal malleolus, the disease spreading thence to the parts of the body already noted. Since the appearance of the first ulcer the patient has never been free from the malady. Some two or three years ago an unusually virulent and destructive lesion appeared under the nail of the left thumb, for which the terminal phalanx of that member was amputated by her medical attendant, all other means taken to prevent the spread of the ulcer having been without avail. During her stay in the hospital new lesions made their appearance almost daily, at first upon the flexor surface of the forearms, later upon the inner surface of the right thigh. They began either as small, pale-red, slightly elevated papules which within a very few hours were replaced by pin-head-sized, flaccid vesicles capped by a small black crust, or they were vesicular from the beginning, with a minute black or brown crust upon the summit. They grew rapidly, attaining the size of a large pea within twenty-four hours; the central black eschar became depressed as it enlarged, and the whole lesion after two or three days resembled closely a vaccination vesicle six to eight days old. Unless excised or destroyed in some manner they continued to enlarge in all directions, the borders being very firm to the touch, while the centre was occupied by a constantly growing, dry gangrenous mass, which was in time loosened by suppuration occurring beneath it. It should be remarked here that this suppuration was evidently a secondary process, appearing only after the eschar had reached a considerable size. There was remarkable uniformity in the character of the lesions. As has already been mentioned, for the first few days they were vacciniform in appearance; after the separation of the central eschar they became sharp-cut, round ulcers with elevated firm borders, spreading in depth and circumference, the bottom covered by a grayish or black slough. Although the disease was not attended by any constant general disturbance, the patient was subject to occasional attacks of severe chills followed by elevation of temperature—sometimes amounting to as much as 104° F.—and diarrhœa, these rarely lasting more than a day or two.

Microscopical examination of a number of excised lesions varying in age from twenty-four hours to five days showed that the disease involved the entire thickness of the skin. In the centre of the lesion the epidermis was transformed into a homogeneous, uniformly staining mass, which blended insensibly with the corium beneath; upon the sides it was lifted bodily from the papillary layer, forming cavities filled with small quantities of coagulated fibrin, degenerating epithelium, and cellular débris. The entire thickness of the corium was occupied by numerous hemorrhages and an enormous number of lymphoid cells, except in the

centre of the lesion, where it had been changed into a mass in which formed elements were no longer distinguishable; in the older lesions

FIG. 3.



Section of day-old lesion containing numerous bacilli.

FIG. 4.

Same as Fig. 3, high power.

the papillary layer was completely disintegrated. Far more interesting and significant, however, was the finding of great numbers of bacilli in the lowest layers of the rete and in the papillary and subpapillary portions of the corium, where their growth had resulted in the almost complete destruction of the tissues. These micro-organisms occurred scattered about irregularly or in considerable masses, resembling morphologically the bacillus tuberculosis, staining best with gentian violet employed after the method of Weigert; all other methods and stains tried either failed completely to stain them or gave very inferior results. Beside this bacillus the ordinary staphylococcus pyogenes aureus was present in large numbers. (Figs. 3 and 4.)

The absence of any constitutional symptoms indicating a general infection, and the superficial situation of the bacilli in the early stages of the disease seemed to justify the assumption that the malady was a local one; the limitation of the eruptive lesions to those parts of the body easily accessible to the fingers of the patient suggested the probability that new lesions arose by autoinoculation. Acting upon these assumptions an effort was made to destroy the micro-organisms in the lesions by early intradermic injections of a 5 per cent. solution of potassium permanganate, this agent being chosen, not because it was regarded as the most effective bactericide, but because it could be introduced into the skin in sufficient quantities without danger of undesirable general effects from its absorption. In addition to these injections the skin was to be washed frequently with a 1 : 1000 solution of mercuric bichloride. Four lesions were injected with the permanganate solution a few hours after their appearance, with the effect of materially retarding their development, but the patient left the hospital too soon to determine whether they were completely aborted. Various forms of treatment had been tried before the case came under my care, but the only effective one had been excision. When the lesions were thoroughly excised, together with a considerable margin of sound skin, the wound thus made rapidly healed; if, however, all of the infected tissue was not removed, as happened frequently, the wound speedily became a steadily enlarging gangrenous ulcer with firm elevated borders, precisely like those which resulted from untreated lesions.

In most of the cases of infectious gangrene of the skin the disease commenced as an eruption of papules, vesicles, or pustules, usually small in number, which enlarging were transformed into eschars, beneath which circular, more or less deeply penetrating ulcers with a marked tendency to spread, occurred. The infectious variety is rarely so prolonged in its course as the trophoneurotic form, but that there are exceptions to this rule is proven by the case just reported. Severe constitutional symptoms, such as high temperature, delirium, extreme prostration, have occurred in a considerable proportion of the cases; in one case the disease terminated fatally.

Multiple gangrene may occur as a complication or sequel of some other acute infectious malady. Demme[1] has reported two cases of this character occurring in children who were the subjects of a severe attack of erythema nodosum, which was apparently contagious, since three children of one family were attacked by it at short intervals. The erythema was accompanied by chills, high temperature—40.2° C. —vomiting, and extreme pains in the legs and arms. One week after the beginning of the attack vesicles, which shortly became pustules, appeared upon the lesions of the erythema, and these in turn were transformed into gangrenous sloughs. A bacillus was found in the lesions, which when cultivated and inoculated into guinea pigs produced a gangrene of the skin like that observed in the children.

Three cases of gangrene of the skin complicationg measles have been reported by Mensi.[2] In the gangrenous lesions were found the staphylococcus pyogenes aureus, a bacillus culturally and morphologically like the proteus vulgaris, and a bacterium resembling the diphtheria bacillus of Loeffler. Inoculation of guinea-pigs with bouillon cultures of the first two produced ulceration like that from which they were originally obtained.

Under the title "A New Species of Gangrene of the Skin with the Formation of Pustules," Rotter[3] has reported a case of gangrene affecting a considerable area of the skin of the leg, which at the end of the second week was associated with an eruption of large hemorrhagic pustules, which continued to appear for fifteen months. From pus from the ulcerating surface and the pustules a bacillus was cultivated, which by reinoculation produced upon the patient lesions like the original ones.

Welsch[4] has recently published a fatal case of cutaneous gangrene occurring in the person of a man who was addicted to the use of morphine hypodermatically, the initial lesion appearing at the site of an injection. From the lesions, which began as abscesses but later became gangrenous ulcers, a bacillus was cultivated which was markedly pathogenic. Simon[5] has likewise reported a case of abscesses and gangrene occurring in a young woman, a victim of the morphine habit; when deprived of her syringe the disease disappeared, but returned when she got possession of it again. Although no micro-organisms were found in this case—probably because they were not looked for—the probabilities are greatly in favor of its being etiologically identical with the one reported by Welsch. As multiple cachectic gangrene, Eichhoff[6] has published a case occurring in a child one and one-half years old, in which, two weeks after an attack of measles, an eruption of dark-red spots, blebs with cloudy contents, and deep ulcers with sharp-cut bor-

[1] Fortschritte der Medicin, 1888.
[2] Gazetta Med. de Torino, 1894.
[3] Dermatologische Zeitschrift, 1895.
[4] Archiv f. Dermatologie und Syphilis, Bd. xxxix.
[5] Breslauer aerztliche Zeitschrift, 1879.
[6] Deutsche medicinische Wochenschrift, 1884.

ders, appeared. Many of the ulcers were covered with dry, black eschars. There was also a marked conjunctivitis with swelling of the lids and purulent secretion. Microscopical examination of material obtained from the bottom and edges of the ulcers revealed a quantity of fungus corresponding in size and appearance with the trichophyton tonsurans, the quantity of mycelium being remarkable. The conjunctivitis was also mycotic. Eichhoff believes that two cases presenting similar clinical features, which he had seen some time previously, and one of which he had reported as an example of cachectic gangrene, were due to the same cause.

In addition to the foregoing cases, in which the presence of a pathogenic micro-organism was positively demonstrated, there remains a small number in which the clinical features of the disease correspond so closely with those of proven infectious nature that they may reasonably be included in the same category, although no micro-organisms were found in them. Hallopeau and Le Damany[1] have described a case characterized by the development of red nodules in the centre of which a yellowish crust formed after loosening of the epidermis; beneath this crust ulcers with sharp-cut, perpendicular edges and covered with putrilaginous detritus appeared, which enlarged peripherally. Some of these lesions remained superficial and healed rapidly, others became covered with a dry black eschar, or becoming markedly indurated extended into the deeper parts of the skin. Along with these ulcerative lesions the lymphatic glands suppurated, giving rise to necrotic ulcerations. The buccal and guttural mucous membranes were affected as well as the skin. The authors reject the idea of a trophoneurosis in this case, but believe the malady to have been infectious, the lesions multiplying by autoinoculation.

Boeck[2] has published the details of a case of multiple gangrene in a child, ten months old, which began as red, slightly elevated spots upon the back, breast, scalp, and upper extremities, upon the summits of which vesicles quickly appeared. When these vesicles reached a certain size the centre became depressed and a brownish crust formed, the lesion at this stage resembling closely vaccine pustules nine or ten days old. The crust continued to enlarge until it included the whole lesion, not being simply dried epidermis, but formed by a more or less deep gangrene of the corium. Numerous micrococci were found, but, as these did not differ from those present in all inflammatory foci in the skin, no special significance was attached to them.

Janovsky and Mourek[3] have quite recently published a case of cutaneous gangrene which began with an eruption of flat, pale-red, hard

[1] Annales de Dermatol. et de Syphilig., 1895.
[2] Archiv f. Dermatol. u. Syphilis, 1882.
[3] Archiv f. Dermatol. u. Syphilis, Bd. xxxv. 1896.

and elastic papules surrounded by a red border. Some of these after enlarging disappeared, leaving the skin slightly pigmented and scaling; others became covered in the centre with a brown or blackish, lamellated, tightly adherent eschar, beneath which was an ulcer with slightly elevated border and steep sides. Repeated examinations of the secretions beneath the crusts and of the blood failed to reveal any micro-organisms. Notwithstanding the failure to find these, the authors do not reject the infectious origin of the malady, since disease of the blood-vessels, syphilis, or other constitutional disease was not present, and the most careful examination of the nervous system failed to discover any ground for belief in its trophoneurotic nature.

Lastly, I would include among the cases of infectious gangrene those of varicella gangrænosa, of which a considerable number have been reported since Mr. Hutchinson first called attention to the malady.

THE CLINICAL SIGNIFICANCE OF REDUPLICATION OF THE HEART-SOUNDS.

By Henry Sewall, Ph.D., M.D.,
PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY OF DENVER; VISITING PHYSICIAN TO ST. LUKE'S AND ARAPAHOE COUNTY HOSPITALS, DENVER.

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Personal Observations. It is curious how all but the grosser physical phenomena escape a clinical observation which has not the habit of noting the apparently unessential as well as manifestly important occurrences. The present writer failed to notice reduplication of the heart-sounds in normal subjects until about four years ago, when, on theoretical grounds, it seemed that there should be perceptible doubling of the second sound of the heart, and, on looking for it, the phenomenon was observed. This sound-character was, for a while, casually noted as a physiological curiosity, but, ere long, observation seemed to show that its study might lead to results of importance to both the physiologist and the clinician. At all events, it appears that much of the confusion in the explanation of the physical signs arising from pathological conditions of the circulation is abolished by the views here presented. In this study it was soon found that attention could not be restricted to the comparatively simple phenomenon of reduplication of the second sound, for the much more difficult task frequently presented itself of explaining the reduplication of the first sound of the heart. Here, too, there seems reason to believe that the conclusions are not without importance. The present work, like all that has gone before it, too often suffers from the necessity of leaving, as final, theoretical explanations which are unfounded on physiological demonstration and which, from the nature of the phenomena, cannot be proved by post-

mortem findings. It is, nevertheless, an attempt to apply known facts of physiology to the solution of problems arising from the clinical study of the heart.

Reduplication of the First Sound of the Heart. *Grades of reduplication.* Reduplication of either heart-sound may have every possible degree of completeness. The normal first sound of the heart may be graphically represented as a curve, like the familiar curve of muscular contraction, rising from a base line gradually to a maximum and then as gradually declining. The first approach toward reduplication is manifested in a prolongation of the period during which the curve maintains its maximum height. The next grade witnesses a slight depression in the highest part of the curve—that is, the first sound has two maxima separated by an interval of less intense sound. In a selected series of cases the notch in the sound-curve may be represented as cutting deeper and deeper until, in certain instances, the curve is completely divided, and we have the normal single first sound split into two sounds separated by an interval of silence. This latter phenomenon is comparatively rare, and probably is usually, if not always, the result of some morbid anatomical change, such as the existence of pericardial adhesions. But incomplete splitting of the first sound, particularly of the slight grade in which two maxima are barely noticed in it, is a common phenomenon. Potain, as quoted by Sansom, considers that doubling of the first sound can be detected in at least one-fifth of healthy subjects, whereas Sansom and some others think it a fact of great rarity. In 205 cases in which I have noted the presence or absence of reduplication, the first sound is recorded as being split or doubled in thirty-five cases. In only two or three of these subjects was the first sound completely divided by an interval of silence. It should be remarked that the lower pitch and longer duration of the first sound of the heart render the recognition of its reduplication much less easy than in the case of the second sound, whose maxima are separated by the same interval.

Difference between real and simulated reduplication of the first sound. It is a happy phrase by which Sansom characterized many cases of reduplication as due not to real repetitions of the normal sound-producing process, but to abnormal events which cause sounds *simulating* the normal cardiac sounds. In the subsequent consideration of the second sound of the heart no difficulty will be experienced in separating real from simulated reduplications. But difficulties arise in considering the first sound from the lack of certain physiological knowledge as to the causes of that sound. It will, for convenience, be here assumed that the first sound of the heart is purely muscular in origin, without in the least denying that, under normal conditions, the sound owes part of its intensity to vibration of the auriculo-ventricular valves or the

chordæ tendineæ. Under this dogmatic assumption, the reduplication of the first sound must mean that the muscular note has a double maximum with a more or less decided contraction pause between.

Real reduplication of the first sound due to non-synchronous contraction of the ventricles. Personal observation has about convinced me of the correctness of the views of Potain and of W. H. Broadbent, that reduplication of the first sound is due, usually, to lack of synchronism in the contractions of the ventricles. There are several reasons for this belief. In 1881 the present writer, in company with F. Donaldson,[1] showed that when the heart of a terrapin was laid bare and supplied with an artificial current of blood, that auricle which received the blood directly, and therefore endured the greater internal pressure, began its systole before its fellow. This but conformed with the well-known fact that intracardiac pressure, up to a certain degree, is a stimulant to the heart. It would be strange if the two ventricles, considering the varying ratios of pressure within them, would not occasionally manifest partial asynchronism. Physiologists are, moreover, familiar with the fact that in the dying heart excitability of the right ventricle lasts longer than that of the left.[2] Again, as pointed out by Broadbent, perception of the reduplication of the first sound is clearest when the stethoscope is applied to the chest over the line which probably corresponds with the position of the ventricular septum, and the double sound gradually becomes single to the right or left of this line, though the double character is usually maintained further in the former direction. The differential stethoscope is of considerable value in localizing the origin of the elements of the reduplicated sound. This instrument, as is well known, can readily be devised by removing the chest-piece from an ordinary flexible, binaural stethoscope and fitting to the ends of the rubber tubes thus set free two conical ear-specula. The apparatus is thus converted into two instruments, one connected with either ear. When one of the bells is placed somewhat to the left of the apex of the heart and the other near the left border of the sternum, the two elements of the double first sound may sometimes be heard nearly separately in the two ears, and the precedence in time of one element over the other can be distinguished. In one case of extreme valvular lesions, in which I was able to be sure of this time-relation, the sound from the left ventricle distinctly preceded that from the right. Some of my cases which were most laboriously studied, and which exhibited the most extraordinary reduplication of both sounds of the heart, are not available in this discussion, because no theoretical explanation of the phenomena could be made unassailable. In one such case the four heart-

[1] Sewall and Donaldson. On the Influence of Variation of Intra cardiac Pressure upon the Inhibitory Action of the Vagus Nerve. Journal of Physiology, 1880–82, vol. iii. p. 361.

[2] Bradford and Dean. The Pulmonary Circulation. Journ. of Physi., 1894, vol. xvi. p 76.

sounds were distinctly separate and similar in duration and quality; scattered through the prolonged systolic phase, they resembled the pattering of rain on a roof. Such extreme reduplication I have only noticed in extreme dilatation, with probable pericardial adhesion, with or without valvular incompetency. That reduplication of the first sound may occur in a marked form in an anatomically normal heart, I have had opportunity of proving by post-mortem examination.

A man, aged forty-seven years, seen at the end of the first week of a mild attack of typhoid fever, exhibited marked reduplication of the first sound nearly limited to the apex region. There was no evidence of nephritis or other complication. Ten days later, while apparently recovering, he suffered an intestinal perforation, for which an operation was performed. The patient died three days later from general peritonitis. The autopsy revealed but three intestinal ulcers, two of which were perforated (one of the perforations having probably occurred subsequent to the operation). The heart was practically normal, except for a slight thickening of one of the aortic valve segments, and very slight congestion of the upper surface of the tricuspid valve.

It is important to notice that in true reduplications of the first sound —that is, those presumably due to non-synchronous contraction of the ventricles—the two sound-elements are of the same "muscular" quality.

In a female patient, aged fifty-nine years, whom I have had under observation some four years, there was, when first seen, considerable hypertrophy of the left ventricle, with powerful murmurs indicative of mitral insufficiency, accompanied by some stenosis. The patient has fared comparatively well, and the murmurs have nearly completely disappeared; but compensation has been maintained not by any improvement in the mitral apparatus, but by an enormous hypertrophy of the left ventricle, whose sound, impulse, and area of dulness reach nearly to the region under the left scapula. Repeated examinations fail to show evidence of aortic regurgitation. My explanation of the great diminution of the mitral murmur is that the mitral valve has been thrown practically out of service through combined shortening of the *chordæ tendineæ* and dilatation of the auriculo-ventricular orifice, compensation being fairly maintained by accompanying hypertrophy of the left ventricle. The first sound at the apex, though much fainter than might be expected, has its normal quality, though it is presumably unmixed with a valvular element and is unconfused with the murmur. For a certain period, the first sound of the heart at the supposed apex in the ninth intercostal space back of the posterior axillary line was distinctly double, the murmur being hardly audible. It was made certain that the cardiac impulse against the chest-wall began with the second element of the double first sound. But three explanations of this fact present themselves: 1. The first element of the double first sound may have been due to sudden tension of the mitral curtains, as in the explanation of reduplication advanced by Sansom. But I have shown reason to believe that the mitral valve was incompetent to produce such a sound. 2. The two ventricles may have experienced non-synchronous contraction, the right preceding the left. 3. The left ventricle may have completed its contraction in two spasms, coming in con-

tact with the chest-wall only during the second phase. This explanation will be considered in the following section.

Reduplication of the first sound due to hypothetical double contraction of the ventricle. In physiological experiments upon the exposed heart, whether of the frog or mammal, it is often witnessed, particularly when the heart labors against abnormally high resistance, that the systole of the ventricles is completed not by a single wave of contraction, but by two distinct efforts, as if two contraction waves were superimposed one upon the other. Under normal conditions nothing of this can be detected with the unaided eye; but the evidence of physiological experiment is corroborative of the suspicion that the cardiac systole is readily broken up into two phases of energetic contraction separated by a phase of comparative rest. In a series of careful experiments, Rolleston[1] measured in dogs the endocardial pressure within the left ventricle. In certain cases, in which the resistance was suddenly raised by compression of the thoracic aorta, the tracings representing variation of endocardial pressure often show the normal wave, which should reach the *nil* point of pressure in diastole, to alternate with smaller, briefer double waves in which the diastolic pressure is far above the *nil* point. This same form of double wave with high diastolic intracardiac pressure is observed in tracings taken from hearts in which the aortic valves have been purposely broken through. The only obvious explanation of the fact is that the ventricle has completed its contraction in two spasms.

In a masterly series of experiments, Roy and Adami[2] proved that the normal mammalian ventricles at a certain period in their contractile movement submit to a pause for a small fraction of a second, as manifested by a slight nick or shoulder in the ascending limb of the contraction-curve. Their experiments, performed chiefly on dogs, were conducted in the following manner: through a window in the front wall of the chest the heart was exposed and the movements of the ventricular wall were graphically registered by a lever attached by a thread to a hook fastened in the ventricular wall. Simultaneous records were made of the contraction of the papillary muscles by means of a hook passed through the wall of the left auricle and caught in the middle of the edge of one of the mitral flaps. The graphic tracings showed that the systole of the ventricle begins before the contraction of the papillary muscles; the sealed slit of the mitral valve must, at that time, be pushed to a greater or lesser distance into the left auricle. The contraction of the papillary muscles then occurs[3] and the mitral valve is

[1] H. D. Rolleston. Observations on the Endocardial Pressure-curve. Journal of Physiology, 1887, vol. viii. p. 235.

[2] Roy and Adami. Heart Beat and Pulse Wave. Practitioner, 1890, vols. xliv. and xlv

[3] The discovery of Roy and Adami as to the relations of the activity of the muscle of the papillæ and of the cardiac wall offers a satisfactory explanation of a puzzling clinical phenomenon. It is often noticed, namely, that the murmur of mitral regurgitation does not attain

suddenly pulled down, greatly increasing the intra-ventricular pressure, of which the walls of the ventricle give evidence by a momentary cessation of movement. The authors also found that this sudden increase of intra-ventricular pressure gave the needed impulse for the opening of the sigmoid valves. Now, it seems not improbable that, under so-called pathological conditions, the duration of this pause in ventricular contraction should be so increased as to become directly perceptible to the senses. If this pause in the systolic movement of the ventricle reached a certain duration, it would be evidenced, clinically, by a doubling of the first sound of the heart. The above theoretical considerations are thrown out as a possible explanation of some cases of reduplication, but the matter will receive no further attention, for the reason that clinical verification of the hypothesis is wanting.

Some conditions determining true reduplications of the first sound. Like other observers, I have sometimes found splitting of the first sound to accompany change in the position of the body. In a case of slight relative insufficiency of the mitral valve and a rather weak heart, and in another showing partial incompetence of the aortic valve, changing from the recumbent to the erect position caused the single first sound to become obviously double. A somewhat similar phenomenon has been observed in practically normal subjects. A patient suffering from a mild attack of typhoid fever, whose heart was normal except for an unexplained dilatation of the right side, showed while lying on the back a normal single first sound, which, however, became double when he turned on the right side. In this case the reduplication occurred at the end of inspiration, instead of at the end of expiration, which, as stated by Potain, is the respiratory phase in which reduplication of the ventricular sound commonly occurs. The results of physiological experiment are very suggestive as throwing light on the relations of reduplication of the heart-beat to blood-pressure; but the clinician must beware of interpreting too fully the complex phenomena which he would analyze by conclusions drawn from relatively simple experiments, the conditions of which are under exact control. Martin[1] and his pupils at Baltimore proved that the dog's heart, physiologically isolated and supplied with an artificial current of blood, did not change its rate of beat under enormous variations of aortic resistance. Marey

its maximum intensity for a perceptible period after the beginning of ventricular systole. Indeed, in some cases, the murmur does not begin until the first sound has become well developed—that is, it is distinctly *post-systolic*. If we admit the fact that the papillary muscles do not begin their contraction until the contraction of the walls is well under way, we must also allow that at that period the murmur must reach its maximum intensity, because then the edges of the insufficient mitral valve are sharply pulled down against the regurgitating current, establishing the most favorable conditions for their vibration. As I recall cases in which the post-systolic character of the murmur was prominent, they seem to have been cases in which little sclerosis of the papillary muscles would have been suspected.

[1] Martin et al. Studies from the Biological Laboratory of Johns Hopkins University, 1878-84

had previously shown that when the vagus nerves were intact every increase of arterial pressure was accompanied by a slowing in the rhythm of the beat due to reflex inhibition through the vagi. In the work with Donaldson previously quoted the writer found that, in the heart of the terrapin, increase of intracardiac pressure within what might be considered physiological limits had perceptible influence in diminishing the cardio-inhibitory action of the vagi. Now, if one but assumes that the two sides of the heart are independently innervated, it should follow that increase of arterial resistance in the aorta or pulmonary artery would cause reflex retardation of action in the left or right ventricle, respectively. On the contrary, increase of diastolic intracardiac blood-tension on either side of the heart might be expected to release that side of the heart from its presumed tonic inhibitory balance and hurry the commencement of its systole. The effect of respiratory movements upon the filling of the heart will be discussed in a later section. Though such speculations have their chief value as working hypotheses, clinical observation supports the view that intracardiac pressure is a controlling influence in regulating the rhythm of heart-action. In pulmonary emphysema, mitral stenosis, mitral and aortic regurgitation, the first sound is very apt to be double. These are conditions in which pulmonary blood-pressure and, at times, right-sided, diastolic intracardiac pressure are increased above the normal. I have also observed doubling of the first sound in several cases of aortic aneurism. It is interesting to note, preliminary to later discussion of the subject, that, in this splitting of the first sound at the septum near the apex, the second sound at the base of the heart usually becomes single as well as accentuated. When, however, ventricular reduplication is very decided, the second sounds at the base become widely separated, because each set of sigmoid valves closes in co-ordination with the relaxation of its own ventricles. In reduplication of the first sound caused by asynchronism in contraction of the ventricles, the first element of the sound seems, as a rule, to correspond with the systole of the right ventricle. In other cases, however, it has appeared as if the left-ventricle sound was heard first. It is extremely difficult to obtain certain evidence on this point.

In an important research by Roy and Adami,[1] on the failure of the heart from overstrain, these authors show experimentally that, at least in the dog's heart, physiological dilatation is readily brought about by increasing the resistance against which the heart empties itself. They assert the incorrectness of the ordinary physiological teaching, according to which the ventricles completely empty themselves at each sys-

[1] Roy and Adami. Remarks on Failure of the Heart from Overstrain. British Medical Journal, December 15, 1888, p. 1321.

tole, whatever the degree of arterial resistance. They show that, when aortic pressure in the dog is artificially raised much above the normal, a residuum of blood remains in the left ventricle at the end of systole. The amount of this residual blood may so increase as to produce a "physiological dilatation" of the ventricle and functional incompetence of the mitral valve. Such demonstrations suggest the great frequency with which, in structurally normal hearts, the conditions of intracardiac pressure may simulate those of organs suffering from permanent valve lesions. Such conditions also come into and complicate the study of sound-reduplications as influenced by intracardiac pressure. Roy and Adami also bring out the important fact, to which we will return later on, that with increase of arterial resistance the moment of opening of the semilunar valve is proportionately delayed. Thus, clinically, we have to consider the balance between the acceleration of contraction of either ventricle, and of the sound caused thereby, probably occasioned by the pressure in it of residual blood and the retardation of the second sound due to late opening of the corresponding sigmoid valve.

Significance of reduplication of the first sound in otherwise normal hearts. True reduplication of the first sound in healthy persons or when it readily appears in disorders not directly involving the heart is, in my experience, significant of circulatory incoördination of some kind, which is manifested by a tendency to fainting, dizziness, or precordial pain. So frequently has this association been observed that it is a common inquiry, when reduplication of the first sound without apparent cause is found, "Do you ever faint?" In a large proportion of cases the answer is affirmative.

Simulated reduplication of the first sound caused by late closure of the mitral valve. Such a condition ought possibly to be classed as a cause of *true* reduplication. In a previous section it has been stated that Hayden considers isolated, audible valve closure to be the normal cause of reduplication. According to Sansom's explanation, the *first* element of the double first sound is of valvular origin. I have recorded a single case in which the two elements of the double first sound of the heart seem to consist, respectively, of muscular and valvular components, the valve-sound forming the second element.

Reduplication of the first sound has been observed in this patient for more than two years. He is the victim of chronic pulmonary tuberculosis, with considerable cirrhosis of the left lung. He is subject to frequent fainting fits, supposed to be attacks of *petit mal*, and also of more serious seizures of the same kind. The area of cardiac dulness seems slightly enlarged though difficult to map out. Numerous careful examinations coincided in giving the following results. The first sound of the heart was frequently widely doubled throughout the cardiac

cycle, the second sound at the base being only slightly split at the end of inspiration. The reduplication of the first sound was most evident and loudest at the apex and a little to its right, being hardly noticeable at the base of the heart. The reduplication would gradually fail when the patient was at rest, breathing quietly. It immediately reappeared after a quick walk around the room or, if reclining, when a deep movement of either inspiration or expiration was made, and would often appear on rising from the recumbent to an erect position. The *quality* of the two elements of the first sound was strikingly different: the first element was muffled, low, and distinctly "muscular" in quality; the second was sharp, higher pitched, and "valvular." When the patient was in repose, and the first sound was single, this was accompanied by a soft systolic murmur loudest at the apex and slightly transmitted to the left (a very thick pleura no doubt interfered with the transmission).

When the first sound became double the murmur began with the first element of the double sound, and continued until the second (valvular) element was heard, when the murmur abruptly ceased. The apparent explanation of these results is as follows: For some unknown reason there was, under conditions of repose, functional incompetence of the mitral valve manifested by a systolic murmur accompanying the single first sound of the heart. But, through a little extra stimulation of the heart, the mitral flaps could be sharply brought together, though at a late period in the systole, and of course the regurgitant murmur would abruptly cease with that closure. Roy and Adami, in their work cited above, show that the mechanism of the papillary muscles is largely independent of the general muscular machinery of the heart, and it is worth suggesting that temporary murmurs, as well as isolated valve-sounds, may partly result from partial paralysis or functional weakness of the former structures.

I have several times noticed reduplication of the first sound, which seemed best explained by supposing that an audible valve-sound was produced by the "post-systolic" contraction of the papillary muscles; in these cases there was low arterial tension.

Simulated reduplication of the first sound produced by impact of the pulmonary artery against the chest-wall. Trustworthy observations are wanting to show the normal relations of the pulmonary artery to the chest-wall. Haycraft and Paterson,[1] from a study of frozen sections of dogs' chests, the heart having been killed in different phases of its cycle, conclude that the base of the heart recedes from the chest-wall during its systole. The fact, however, that the great arteries were

[1] Haycraft and Paterson. The Changes in Shape and in Position of the Heart during the Cardiac Cycle. Journal of Physiology, 1896, vol. xix. p. 496.

emptied previously to making the sections totally invalidates their conclusions, it being well known that the empty vessels pull the base of the heart upward and backward. W. Jenner[1] long ago showed that in human subjects, with shallow, flexible chests, cardiac murmurs could readily be generated by pressure with the stethoscope over the base of the heart. Constriction of the pulmonary artery was, no doubt correctly, ascribed as the cause of this phenomenon. With arteries full of blood, as in life, the basal rim of the heart must lie nearer to the chest-wall than is the case after death; also, with a distended left auricle the base of the heart is probably lifted forward. Roy and Adami[2] showed that in the dog's heart during the systole of the ventricles the anterior surface at the base comes closer to the chest-wall. When the chest of a mammal is opened and the beating heart is directly observed, the most extensive cardiac movement is one imparted by the two great basal arteries. When the ventricles shoot their contained blood into the already distended aorta and pulmonary artery, these vessels suddenly elongate under the increased strain, their lateral enlargement, as pointed out by Roy and Adami, being insignificant. It is admitted by all physiologists that the arteries in lengthening push down the base of the heart. The aorta springing nearly from the centre of the base and the pulmonary artery from its anterior circumference, the systolic push of the arteries would be expected to preponderate on the anterior segment of the base. As a matter of fact, this expectation is realized, for when the beating heart is directly observed the base has a nodding motion, as if its plane inclined forward and apexward at every systole. If the arteries are gradually emptied by bleeding the animal, the basal motion of the heart becomes proportionately less. The foregoing considerations make reasonable the supposition that, under certain conditions, the base of the pulmonary artery might at each systole of the heart strike against the front wall of the chest. Moreover, since the sigmoid valves are not open, and consequently the basal arteries do not elongate until a longer or shorter interval after the beginning of ventricular contraction, the sound of the blow upon the chest-wall should form the second element of the split first sound. The time interval elapsing between the beginning of ventricular contraction and the opening of the semilunar valves is said to be very variable. The extent to which the first sound is divided must vary in proportion. I have sometimes felt convinced, while making physical examinations of the chest, that apparent reduplication of the first sound was the result of impact of the pulmonary artery being superadded to the sound of ventricular contraction. The differential points in favor of this belief are: 1. The

[1] W. Jenner. Medical Times and Gazette, 1856.

[2] Roy and Adami. Heart Beat and Pulse Wave. Practitioner, 1890, vols. xliv. and xlv.

greatest intensity in the sound of the reduplication is found over the probable origin of the pulmonary artery. 2. In this area there is an impact, the chest-wall being moved outward, systolic in time. 3. The reduplication is usually plainest at the end of expiration (when the lung is least interposed between heart and chest-wall). 4. The second element in the split sound becomes louder with deeper pressure of the flexible stethoscope, which, as I have tried to show in another place,[1] indicates that the sound-producing body is in contact with the chest-wall. I am not yet prepared to state the clinical significance of simulated doubling of the first sound of this character.

Simulated reduplication of the first sound due to audibility of the auricular contraction. A typhoid fever patient, as a result of over-exertion early in convalescence, suddenly collapsed with symptoms of heart-failure. His heart, examined during the subsequent period of prostration, showed a marked increase toward the right in the area of precordial dulness. Fairly limited to the upper, right-hand corner of this area, under the third right costal cartilage and corresponding, probably, to the site of the right auricle, the sounds of the heart assumed a gallop rhythm.[2] This rhythm was composed of three elements, the third being the normal second heart-sound, the second the normal first heart-sound, and the first an abnormal sound immediately preceding the normal first sound. The impression given to the ear and the circumscription of the presystolic sound led to the suspicion that the first element of the triple sound was due to a labored and sonorous contraction of the auricle. After a few days the heart-sounds recovered their normal character. Few observers agree with Dr. Johnson[3] in attributing ordinary reduplication of the first sound to audible auricular contraction.

THE SECOND SOUND OF THE HEART AND ITS REDUPLICATION. *Cause of the second sound of the heart.* No one disputes the view that the second sound of the heart is due to vibrations originating in the pulmonic and aortic semilunar valves. Without going too minutely over familiar ground, it may be repeated that there is no doubt that the sudden tension of the sigmoid valves, which produces the second heart-sound, is also due to the reflux against the valves of the blood-wave which the ventricle in its systole has imparted to the arte-

[1] Sewall. Clinical Uses of Stethoscopic Pressure in Examination of the Heart. New York Medical Journal, 1897.

[2] The so-called "gallop rhythm" is usually described as composed of three sound elements occurring in the same cardiac cycle. It has sometimes seemed to me that the elements were four in number. The elements of reduplicated sounds are by no means necessarily separated by time intervals such as to give to the ear the impression of the gallop rhythm. The occurrence of this rhythm requires special study, and I have purposely avoided using in this discussion *data* derived from it. François-Franck, quoted by Sansom (p. 208), has made a valuable study of the *bruit de galop*.

[3] George Johnson. Lancet, 1876, vol. i. 699.

rial system.[1] The time which elapses between the emptying of either ventricle and the stroke of the reflux wave upon its sigmoid valve must depend, at least, upon the following factors: 1. The length of time occupied by the ventricle in emptying itself, as determining the starting time of the positive arterial wave. 2. The arterial elasticity, as determining the rate of reaction of the arterial walls. Arterial elasticity may be said to depend (*a*) on the structure and thickness of the arterial wall; (*b*) on the amount of strain or tension to which it is submitted. The first element (*a*) is, in a given case, invariable; the second (*b*) is variable. 3. The length of the arterial tube through which the positive wave progresses; this may also, for practical purposes, be regarded as a fixed quantity, the reflux wave returning more quickly, other things remaining the same, the shorter the arterial path. Two variables are, therefore, to be considered as influencing the moment of sigmoid tension: first, the time taken for the positive wave to escape from the ventricle, and especially the moment of its beginning; second, the height of blood-pressure in the arteries. Notable difference in the times taken by the ventricles to expel their blood must, of course, be evidenced by a reduplication of the first sound of the heart. As to the action of the second variable, it is well to state that the rate of reaction of the arterial wall, and therefore the rapidity with which the reflux wave returns upon the sigmoid valve, increases with arterial blood-pressure, and the second sound succeeds the first sound of the heart at a shorter interval.

Reduplication of the second sound of the heart a normal phenomenon. From the considerations brought forward in the preceding section it is seen that the conditions determining the time of the closure of either set of semilunar valves are not without complexity. Though, according to various experimenters, the aortic as compared with pulmonary blood-pressure has a value of three or five to one, other factors may so hasten rebound of the pulmonary arteries as to make the closure of the pulmonic valve synchronous with or antedate that of the aorta. Physiological and clinical observation must, therefore, be the final resort in determining the relative movements of the two sets of sigmoid valves and the composition of the sound proceeding therefrom. From a great number of observations I venture to make the statement that reduplication of the second sound of the heart, so far from being unusual, is a normal phenomenon, and is to be detected in a large majority of healthy hearts. This reduplication has an infinite variety of degree, passing

[1] It seems very probable, as is suggested by a diagram constructed by Roy and Adami, that practical *closure* of the sigmoid valves occurs at a measurable interval before the reflux wave strikes them, and consequently before the second sound is generated. It is hardly in order here to discuss the reasons for this belief. It is, however, necessary to realize a fact admitted by all physiologists, that the sigmoid valves are firmly shut *before* the ventricles begin to relax in diastole.

from the short, sharp, single second sound through stages in which the second sound is obviously prolonged at the end of inspiration, or faintly exhibits two maxima at this respiratory phase, or, as is usually the case, shows a complete splitting or doubling of the second sound for one or two heart-beats. All observers agree that true reduplication of the second sound is most manifest at the end of inspiration. It is not unusual, in healthy subjects, to find the sound reduplicated throughout the respiratory cycle; the interval between the two elements of the sound is smallest at the end of expiration (when, it will be remembered, reduplication of the first sound, when it occurs, is commonly most obvious); then, as inspiration proceeds, the splitting of the sound becomes more and more obvious until, at the end of inspiration and beginning of expiration, the second sound is widely doubled with a perceptible interval of silence between the two elements. The widest reduplication of the second sound is, however, found in certain pathological conditions, particularly in cases of pericardial adhesions. In such cases I have not been able to observe the same relation between the phase of respiration and the length of the reduplication interval, which is so striking a feature in normal hearts. The degrees of reduplication can be well imitated by striking with the palmar side of two fingers against a wooden surface; every grade of doubling can be represented by letting the strokes of the fingers succeed one another at various intervals.

Time value of the reduplication interval. On the strength of authority which he does not specify, Sansom states that an interval of nine-one-hundredths to one-twentieth of a second may elapse between the closures of the two sets of sigmoid valves. He then asserts that these intervals are too small to be perceived by the ear. No less an investigator than Helmholtz[1] has asserted that at least one hundred and thirty-two separate pulses of air per second, in the form of "beats," can be distinguished apart by the ear. The physical characters of the arterial valve-sounds, their short duration and high pitch, especially fit them to be distinguished apart when separated by a very small interval. In this case probably a much smaller interval of reduplication can be perceived than in the first sound. I have made no effort to measure the duration of the reduplication interval, but it varies from *nil* to a period which seems to the ear to be at least as long as the sound element itself.

Physiological events determining reduplication of the second sound. It is, perhaps, the most commonly accepted opinion that the reduplication of the second sound has its origin in the non-synchronous closure of the two sets of arterial valves. But the fact that so competent an authority as Sansom totally disclaims the sigmoid origin of reduplication,

[1] Helmholtz. Sensations of Tone. Translated by Ellis.

is itself sufficient reason why nothing should be taken for granted in the explanation of the phenomenon. More than a year ago I submitted the question to the test of physiological experiment, resulting in the conviction that reduplication of the second sound is really due to the non-synchronous closure of the aortic and pulmonary valves. Following are abstracts from the notes of two experiments performed on dogs under morphium-ether narcosis:

EXPERIMENT I.—Large dog. Chest shaved. Carotid artery and vago-sympathetic nerve on left side isolated. A fine, stiff brass wire, coiled like a corkscrew at one extremity, was slipped through a slit into the carotid, and the screw end was passed down to the level of the aortic valve. The escape of blood from the artery was, of course, prevented by appropriate ligatures. With a turn or two of the wire the helix passed into the aortic orifice and the valve was prevented from closing. Some of the results were obtained by holding up one of the semilunar flaps by a wire terminating in a fine hook. In this dog the second sound is plainly heard at the left border of the sternum about two inches from the ensiform process. The second sound frequently seems double, especially at the end of inspiration. The first element of the reduplicated sound appears distinctly the louder. With the wire inserted between the segments of the aortic valve, the second sound of the heart is greatly reduced in intensity and becomes *single* (with the murmurs generated by this procedure we have nothing to do). It was subsequently found, post mortem, that the end of the wire had, at times, caught in the posterior wall of the ventricle. When the wire was caught in the heart-muscle in this way it was found to be sharply pulled apexward with each systole of the ventricle, and when it was gently strained in the opposite direction the first sound of the heart became distinctly double, but the second sound remained single, and was heard most plainly at the base of the heart. When the peripheral stump of the vagus nerve is stimulated by an interrupted electric current, the aortic valve being held open, the rate of heart-beat is much slowed, and the single second sound becomes nearly inaudible (because of the lowered blood-pressure in the pulmonary artery). Drawing the wire away from the valve, reduplication of the second sound reappears, again to become single when the valve is held open. When the aortic valve is pushed on from above, and consequently the intra-ventricular pressure is suddenly raised, the first sound of the heart becomes reduplicated at intervals.

EXPERIMENT II.—Large dog, treated as before, but a slit is also made in the abdominal wall so that two fingers can be inserted and compress the aorta. Without manipulation, the second sound is only prolonged, not distinctly split at the end of inspiration. When the aorta is compressed, the rate of heart-beat decreases probably one-half (reflex inhibition), and the second sound becomes double after a few seconds. Removing the compression, reduplication of the second sound persists for about a minute. Release of the aorta is also accompanied by reduplication of the first sound. Again applying pressure to the abdominal aorta, the first sound becomes single and the second double. With the left vagus cut, occlusion of the abdominal aorta causes both heart-sounds to become double, with somewhat of a gallop rhythm.

When the aortic valve is held open and the abdominal aorta is compressed, the second sound remains single, but becomes double when the valve is allowed to close.

These experiments show conclusively that reduplication of the second sound of the heart requires the co-operation of both sets of sigmoid valves. They also indicate that variation of arterial pressure may be an important factor in causing reduplication. Most important of all, there seems reason to conclude that in physiological experiment we have a means of solving many of the problems of cardiac pathology. An interesting clinical confirmation of the bivalvular origin of reduplication of the second sound is found in cases presenting an extreme grade of aortic regurgitation. In such cases the second sound at the base is invariably single, because the sound of aortic closure is absent.

Frequency of real reduplication of the second sound. Sansom[1] considers doubling of the second sound to be a phenomenon which is "extremely rare," and then goes on to enumerate various pathological conditions in which he has noted reduplication. These conditions are precisely those in which my own observations have shown the absence of true reduplication. The discrepancy finds an easy solution in the fact that Sansom uses the term "reduplication" to distinguish only *simulated* doubling of the second sound. As stated above, my observations are in accord with the opinion of those who hold that reduplication of the second sound is practically a normal physiological phenomenon. In one hundred and eighty-four cases, in which the condition of the second sound finds mention in my notes, the sound was reduplicated in eighty-five practically normal hearts, and in eighteen cases of heart-disease. The second sound was single or only prolonged at the end of inspiration in fifty-eight normal hearts and in twenty-three cases of heart-disease. The unity of the second sound in the eighty-one cases was, as will be hereafter explained, in most instances the result of some obstruction in the pulmonary circulation. It should also be mentioned that, when the second sound is reduplicated in disease of the heart involving pulmonary congestion, the first sound is almost sure to be coincidently doubled. These points will be made clearer in a later section.

Area of audibility of real reduplication of the second sound. Sansom asserts that "the area of audibility of the phenomenon (reduplication of the second sound) is not marked at the base of the heart, while it is very manifest at the apex." This statement is misleading, since, as will be pointed out later, the reduplication referred to by this author is, to use his own term, *simulated* and due to wholly different causes from the sounds which originate in the sigmoid valves. I can only affirm that the phenomenon of true reduplication of the second sound

[1] Sansom. Diagnosis of Diseases of the Heart and Thoracic Aorta, 1892, p. 207.

is heard with greatest intensity at the base of the heart, usually under the second and third left costal cartilages bordering on the sternum. Sometimes the perception of reduplication is strictly confined to this area, but often it radiates with diminishing intensity in all directions, more especially downward.

Sansom discards the view that difference of arterial tension in the pulmonary and systemic circuits, respectively, can cause sensible reduplication, "for until the occurrence of diastole there can be no reflux, and consequently no second sound. The cause of the doubling, as of the first, so of the second sound, therefore, must revert to the ventricles. When their systole is perfectly simultaneous, the second sound, produced by the reflux against the semilunar valves of the two great vessels at the moment of ventricular relaxation, must be simultaneous; when the systole is not simultaneous, or does not last through equal periods of time, the diastolic reflux cannot be simultaneous. If the discrepancy be such as can be appreciated by the ear, the second sound is doubled." The author neglects the important fact, supported by the evidence of all physiological experiment, that closure of the semilunar valves, or the reflux against them, does not follow or coincide with the relaxation of their respective ventricles, but precedes it by a relatively considerable interval. It can hardly be imagined that the slight negative pressure sometimes created within the ventricle by its diastolic rebound can have any important effect in directing the inertia movements of the heavy blood-stream.

Sequence of the elements of the reduplicated second sound. It was stated above that it is, at times, apparently possible by the use of the differential stethoscope to find the order of precedence of the two elements of a double first sound when the bells of the instrument, connected with either ear, are placed one over the right, the other over the left ventricle. But, though it is easy to determine in a given case whether a sound is single or double, or even to be sure which of the two elements is the louder, it is extremely difficult, with the small time-intervals under consideration, to apprehend the order of precedence of two different sounds heard one by the right and the other by the left ear. I have made numerous observations to determine the order of sequence of the elements of the double second sound, and, to some extent, their areas of distribution. No conclusions were accepted except as controlled by observations made while the eyes were closed and the bells of the stethoscope were placed by an assistant upon the chest of the patient in positions unknown to the observer. The following extracts from clinical notes illustrate the points in question:

Case I.—Patient, a male child, aged eleven years, with slight digestive disorder. At base of heart the second sound is widely double throughout inspiration. With one bell of the differential stethoscope

applied to the second intercostal space considerably to the left of the sternum, and the other bell to the corresponding space right of the sternum, the reduplication is heard, one element by each ear. The sound comes first to the ear from the bell applied to the right of the sternum.

The sound is cut off from either ear by clamping the corresponding rubber tube, or by firm pressure of the bell upon the chest (as explained in another place[1]). That is, the sound of aortic closure is first in order, and is heard nearly pure in the second right interspace, while the sound of pulmonary closure is found isolated in the second space considerably left of the sternum.

CASE II.—Adult male, subject of extensive pulmonary tuberculosis. Second sound at base of heart is plainly double. In the second costal interspace, two and one-half inches left of mid sternum, the second sound is single (pure pulmonary). In the second interspace, two and one-half inches right of mid-sternum, the second sound is single (pure aortic). A bell of the differential stethoscope is placed on each of these two points, and the second sound appears double, the sound in one ear preceding that in the other. At the apex of the heart the second sound is single. With the bells of the differential stethoscope placed one on the apex and the other in the second interspace three and one-half inches left of mid-sternum, the second sound appears double. With the latter bell transferred to the second right interspace, the apex bell remaining in place, the second sound becomes single. That is, the second sound as heard at the apex is synchronous with that heard under the "aortic cartilage," but precedes that heard in the second left interspace, which is probably due to pulmonary closure.

When both bells are applied to the second left interspace, one close to the sternum, where reduplication is obvious, and the other farther to the left, where the sound of pulmonary closure is alone heard, the *second* element of the double sound is louder. When the bell which is farther to the left is transferred to the pure aortic region right of the sternum, the *first* element of the double sound becomes louder—that is, in the first case the single sound of pulmonary closure has been added to the double sound of aortic-pulmonary closure, and the pulmonary element seems more intense. In the second case the reverse is true, the double sound containing the pulmonary element falls upon only one ear, while the aortic element strikes both ears, and, consequently, appears louder. The precedence of the two stronger sound-elements is reversed in the two cases, and we conclude that aortic closure precedes the pulmonary. I have ventured on this prolix description because it seems that the differential stethoscope is an instrument which should not be neglected in the study of heart-sounds.

Reduplication as influenced by the ratio of pulmonic to systemic arterial pressure. The normal variations of blood-pressure within the pulmonary artery and the conditions determining them are but little known. All authorities agree that the pulmonary and systemic circulations are largely independent of each other. The physiological mechanisms are so adjusted that the pressure within the systemic ves-

[1] Sewall. Clinical Uses of Stethoscopic Pressure in Examination of Heart. New York Medical Journal, 1897.

sels may undergo extraordinary alterations without noticeable influence on the pulmonic blood-tension.

Bradford and Dean,[1] experimenting on dogs, measured the pulmonary arterial pressure through a canula tied in the artery supplying the left lower lobe of the lung. Simultaneous records were made of pressure in the carotid artery. After vigorous artificial respiration the animal breathed, for some seconds, in a normal manner with the right lung. These authors say, "large oscillations of pressure in the systemic arteries produce often little or even no effect on the blood-pressure in the pulmonary artery. . . . The pressure in the lung vessels, however, undergoes a rise when the increase in the systemic pressure is not only considerable in amount, but also of long duration." The authors explain the former result by the great distensibility of the lung-vessels, which can accommodate a great excess of blood without strong elastic reaction of their walls. They also explain the negative influence on pulmonary blood-tension of enormous increase in aortic pressure (produced by compressing the thoracic aorta) as due to efficient working of the left ventricle and of the mitral valve. Bradford and Dean think they have demonstrated the action of vasomotor nerves on the calibre of the pulmonic vessels, though some observers have denied the existence of a pulmonary vasomotor mechanism. At all events, we are in the dark as to the normal relations of pulmonary arterial pressure to vasomotor influences.

Effect of position of the body on reduplication of the second sound. There are two conditions which are to be especially studied as influencing blood-pressure in the pulmonary artery: one is the position of the body and the other the respiratory movement. In a recent valuable communication, Hill and Barnard,[2] experimenting on dogs, came to several conclusions of great clinical importance. These authors fastened the animals under experiment on a table capable of being revolved in a vertical plane. Simultaneous tracings of blood-pressure were taken from the aorta and the superior *vena cava* through glass canulæ passed down the carotid artery and the external jugular vein, respectively. When a dog, narcotized with morphine, but otherwise normal, is placed in the feet-down position, the venous pressure at once falls and remains lowered until the horizontal position is recovered. The arterial pressure, however, is lowered only momentarily, rising to or somewhat above the normal during maintenance of the vertical posture. Hill and Barnard point out that the flow of blood into the heart is under control of the vasomotors of the abdominal vessels and the constricting effect upon

[1] Bradford and Dean. The Pulmonary Circulation. Journal of Physiology, 1894, vol. xvi. p. 76.

[2] Hill and Barnard. Influence of the Force of Gravity on the Circulation. Journal of Physiology, 1897, vol. xxi. p. 323.

the visceral veins exerted by the abdominal walls. They write, "The healthy heart cannot be thrown into paralytic dilatation by the most forcible compression of the abdominal veins. The chloroformed or asphyxiated heart, on the other hand, can easily be thrown into paralytic dilatation by this means. . . . The right heart can be emptied and a state of paralytic dilatation relieved by the simple procedure of dropping the animal into the vertical feet-down posture. This is a valuable method of recovery in conditions of asphyxia or chloroform collapse. . . . The *venæ cavæ* form a constant low head of pressure, from which the heart draws its supply. Thus the diastolic pressure within the heart is kept constant during the enormous changes of arterial pressure which are brought about by vaso-constriction."[1]

In the few observations I have made as to the relation of the character of the second sound of the heart to position of the body, it has appeared that in the normal heart reduplication of the second sound was more marked in the erect than in the recumbent position, while with mitral regurgitation the reverse was the case. In the former condition pulmonary blood-pressure would be relatively reduced by the gravitation of blood from the right side of the heart, while in the latter pressure within the pulmonary system might be supposed to be increased by stronger relative backflow through the incompetent mitral valve, on account of heightened aortic resistance.

But, as might be inferred from the results of Hill and Barnard, conclusions as to the effect of posture on the ratio of pulmonary to systemic blood-pressure must always take into account the functional tone of the visceral bloodvessels and of the abdominal wall.

Effect of respiratory movements on reduplication of the second sound. All investigators admit that the respiratory movements are essential aids to circulation of blood through the lungs. As put by Rollett,[2] the diminution of intrathoracic pressure caused by enlargement of the chest in inspiration must reduce blood-pressure in the pulmonary veins, but has very little influence on the pressure within the thicker-walled pulmonary artery. Therefore, the rate of blood-flow into the left auricle is greatly accelerated. At the same time the great veins and right side of the heart are filled with blood by aspiration. This alone would greatly increase pulmonary arterial pressure were it not for the fact that, with the distention of the lungs by negative pressure outside them, the total capacity of the pulmonary vascular circuit is greatly increased in inspiration.

[1] It is reasonable to suppose that the upright posture of the body, found necessary by so many patients with heart disease, depends upon the relief so gained through gravitation of the blood from the overcharged right heart. It may be suspected that *posture* in heart disease has peculiar diagnostic value, for many who are desperately ill do not seem to require the upright position.

[2] Rollett. Hermann's Handbuch d. Physiologie, 1880, vol. iv. p. 280.

It is well known that tracings of systemic arterial pressure, usually taken from the carotid artery, show remarkable undulations of pressure dependent on the respiratory movements, though it would be an unwarranted assumption to suppose that other important physiological factors do not combine to cause the phenomenon. These respiratory undulations of systemic arterial pressure are not usually parallel in time with the respiratory movements; the waves commonly reach their highest point between the beginning and the middle of the expiratory phase, and the lowest between the beginning and middle of the inspiratory movement. The rise is apparently initiated by events dependent on inspiration, and the fall by conditions involved in expiration. These relations vary somewhat with the depth and frequency of respiration. According to the tracings obtained by Bradford and Dean, the respiratory waves in pulmonary arterial pressure are, in proportion to the total height of pressure, very much higher than the corresponding waves from the systemic arteries. Also, what is very important for this discussion, the respiratory waves in the two arterial systems do not correspond in their phases; that is, assuming the accuracy of their tracings, the highest pressure in the systemic arteries is not simultaneous with the highest in the pulmonary artery.

In an important work descriptive of experiments on dogs with divided vagi, S. de Jäger[1] dwells on the point that the change in the capacity of the pulmonary vessels, combined with the conditions of resistance to blood-flow therein, produced by respiratory movement, all are important in causing the "respiratory" variations in systemic arterial pressure. De Jäger's conclusions are best stated in his own words: "Every increase in the capacity of the pulmonary vessels causes a fall in the arterial (systemic) blood-pressure. Every decrease in the capacity of the pulmonary vessels causes a rise in arterial pressure. Every increase of resistance in the pulmonary vessels causes a fall in arterial blood-pressure. Every decrease of resistance in the pulmonary vessels causes a rise in the arterial blood-pressure.

	During normal respiration.	
	The capacity.	The resistance.
During inspiration becomes . .	Larger.	Less.
During expiration becomes . .	Smaller.	Greater."

We shall probably be right in concluding from the foregoing data that the maximum difference between the systemic and the pulmonary arterial pressures is reached just about the end of inspiration or beginning of expiration. For at this time the respiratory wave of blood-pressure in the aorta is reaching its highest point, while the maximum

[1] S. de Jäger. Experiments and Considerations on Hæmodynamics. Journal of Physiology, 1886, vol vii. p. 130.

inspiratory capacity of the pulmonary vessels has been attained; but the elevation of pulmonary blood-pressure, due to collapse of the lung, has not yet begun. But this is just the time when, from the clinical side, the splitting of the second sound is, when heard, most obvious. It is not intended to deny that cardiac and vasomotor nerve action may have a share in the production of respiratory blood waves. Our conclusions would not thereby be essentially modified.

Alteration of the ratio of pulmonary to systemic arterial blood-pressure under pathological conditions. Increase of pulmonic blood-pressure probably accompanies every condition in which there is increased resistance to the flow of blood through the lungs. Thus, any defect of the mitral valve impedes the emptying of the lungs. In another way, pulmonary emphysema is probably the cause of impediment to the circulation in the lungs and elevation of blood-pressure. Anæmia of the lungs, on the other hand, no doubt results from inefficiency of the vasomotor mechanism of the abdominal vessels, or, in some cases, from laxness of the abdominal walls, allowing blood to settle in the great abdominal veins (Hill and Barnard). Physiological evidence is against the belief that the vasomotor mechanism of the lungs can compensate for any great diminution of blood in those organs, as the vasomotors of the systemic vessels can for the loss of fluid to the greater circulation.

The relation of the two sounds of the heart as to their reduplication. The full significance of the doubling of either sound of the heart cannot be apprehended until the condition of the other sound is determined. I will now assume, as proved, that reduplication of the second sound of the heart depends upon the non-synchronous closure of the two sets of semilunar valves, which is, in turn, dependent on the difference of tension in the pulmonary and systemic arteries as regulating the rate of recoil against their respective valves. When the pressure within the pulmonary system is relatively increased the reflux against the corresponding sigmoid valves is accelerated, and reduplication is lessened or fails. And if, as seems to be frequently the case, the right ventricle is stimulated, by increased resistance or the presence of residual blood within it, to begin its beat before the left, a prolonged or double first sound is heard, and the pulmonary semilunar closure is still more hastened. As a matter of fact, when the first sound has two maxima, or is slightly reduplicated, the second is usually single. Conversely, when the second sound is found to be single, the first is usually double; occasionally only careful search will disclose the double character of the first sound; but it is rarely missed when the more easily distinguished second sound is found to be single throughout the respiratory cycle.

In cases of typhoid fever I have a number of times found the second sound to be single during the first week or two of the disease, while at the same time the first sound was double. As the patient progressed

toward convalescence the second sound gradually became widely reduplicated and the first sound single. As will be seen later, the same clinical changes have been witnessed in pneumonia. If the contraction of the right ventricle precedes that of the left by a sufficient interval, the pulmonary valves will close before those of the aorta, and we shall hear both sounds reduplicated. In a case apparently suffering from pericardial adhesions, in which both sounds were double, the differential stethoscope seemed to show distinctly the sound of pulmonary closure to precede that of the aorta. As a matter of fact, it is always observed that when there is wide doubling of the first sound of the heart, which may be attributed to asynchronism in the ventricular contractions, there is also continuous reduplication of the second sound. Quite different in significance are those reduplications of the first sound caused by the left ventricle contracting before the right or by the right lagging behind the left. In such conditions the natural splitting of the second sound would be favored and the reduplication interval would be widened. Such is usually the case in chronic nephritis, though at times in this disorder a single second and double first sound may be found. In certain stages of nephritis, the first sound being single and the second but slightly split, the small reduplication interval of the second sound may be attributed to delayed opening of the aortic valves due to increased resistance. Curious results have been found in a case of nephritis with heart lesions, in which there were sudden variations in the rate of beat, and also in cases of valvular disease with intermittent beat; reduplication of either sound would come and go with different characters of heart action.

Pathological conditions in which reduplication of the second sound is marked. In cases of chronic nephritis, with high tension in the systemic arteries, reduplication of the second sound has, in my experience, usually been marked. In several cases of appendicitis it has been prominent. Subjects of pulmonary tuberculosis are, as a rule, favorable for observation of the phenomenon. This seems surprising when it is considered that resistance to blood flow in the lungs is probably increased, and that, at the same time, aortic pressure is diminished. But the anomaly is easily explained if we admit that there is also lowered vasomotor tone in the systemic vessels and stagnation of blood therein, thus restraining the return of blood to the right heart. In subjects of somewhat neurotic temperament, particularly females, some of the most striking examples of reduplication of the second sound have been observed.

Pathological conditions in which reduplication of the second sound is absent. The second sound is usually single, or but slightly prolonged at the end of inspiration, in cases of pulmonary congestion or in which resistance to pulmonary circulation is increased. Thus, the second sound is almost

invariably single in emphysematous subjects (a condition in which the first sound is usually prolonged or double). In a fatal case of emphysema with dilated right heart, the turgidity of the jugular veins and the distress of the patient were temporarily greatly relieved by hypodermatic injection of nitroglycerin; at the same time the second sound, which had been single, became reduplicated. In pneumonia, up to and through the acme of the disease, I have observed the second sound to be single, the reduplication reappearing and becoming more and more marked as convalescence proceeded. In cases of mitral regurgitation which are doing badly the second sound is single, though reduplication recurs to a slight extent when compensation and improvement take place. On the other hand, in regurgitation through the tricuspid valves reduplication of the second sound seems to be characteristic. The second sound is recorded as single in most of my cases of active pericarditis, aortic regurgitation, aortic aneurism, and pleural effusion. In numerous cases of hæmoptysis the second sound has been found single, reduplication returning after cessation of the hemorrhage. In a weak but normal heart reduplication of the second sound is often absent.

Simulated reduplication of the second sound of the heart. This is the form of reduplication which has received most attention and which, among most observers, has been confused with true doubling of the second sound. Sansom carefully distinguished between true and simulated reduplication of the second sound, and then decided that the latter condition was alone perceptible to the ear. The sound in question, which seems to be a repetition of the second sound of the heart, always follows the latter, and is separated from it by a shorter interval than removes the second from the first sound. It gives the ear the impression of a *rebound* from the second sound, and, though softer, often resembles it in quality and duration. The sound simulating doubling of the second sound is rarely heard at the base of the heart, but always at the apex or to the right of this point. The area in which it is heard is often strictly circumscribed, and may be limited either to the right or left ventricle, much more frequently the latter. The sound is annulled by gentle pressure with the flexible stethoscope.[1] At times the sound is more prolonged and has a rougher quality over the site of the mitral valve than at the apex. Sometimes, at least, it disappears with deep inspiration and becomes stronger with expiration. This sound is heard only in pathological conditions of the circulation in the heart. Close attention may detect it in a considerable proportion of cases. The simulated second sound attains especial prominence in the lesion of mitral stenosis, and is said to occur in at least one-third of such cases. I feel convinced, however, that the simulated reduplication of the second sound

[1] Sewall. Clinical Uses of Stethoscopic Pressure in Examination of the Heart. New York Medical Journal, 1897.

may, at times, be heard in any condition in which the blood-pressure in either auricle is much in excess of the normal. I have thus found it present in pneumonia, in nephritis complicated with pericarditis, and in mitral regurgitation without evidence of stenosis. Sansom also enumerates several disorders in which he has observed the sound. That view is probably correct which regards the simulated reduplicated second sound as having its origin in the elastic reaction of the overstrained (usually left) auricle which comes into play at the moment the resistance in front is lowered by the diastolic dilatation of the ventricle. The sound is thought by Sansom to be made by the sudden tension imparted to the mitral valve by reflux of the current issuing from the overstrained auricle at the beginning of diastole. Roy and Adami suggest that, in mitral stenosis, the sound is due to the vibration of the free edge of the narrowed orifice caused by the direct passage of the current from the auricle. I have heard the sound under conditions in which there seemed reason to believe that the mitral valve was practically inoperative, and have ascribed it to the sound of impact of the blood against the ventricular wall. This, I understand, is essentially the explanation for the phenomenon given by Potain. It may be observed that in mitral stenosis, in which condition this phenomenon is most common, the aspirating force of the ventricle, greatest at the beginning of diastole, probably produces a greater negativity of pressure within the ventricle than in any other condition. The verification of these theories must await more evidence from the combination of clinical with post-mortem, not to say physiological, observation.

Diagnostic value of the study of reduplication. In the cases in which I have observed simulated reduplication of the second sound I have always made sure that this was not the real reduplication caused by non-synchronous closure of the semilunar valves. This has always been possible by finding in the second or third left interspace the characteristic prolongation or splitting of the second sound at the end of inspiration. No diagnosis of "simulation" in the doubling of the second sound can be certain until the normal splitting of the second sound is recognized as occurring independently. Thus the recognition of the character of the true second sound of the heart greatly facilitates the analysis of the complex signs which strike the ear under pathological conditions. Again, estimation of the reduplication interval in the second sound is of great assistance in the judgment of the tension of the pulmonary bloodvessels. It is well known that, in pneumonia, for example, considerable aid is given the clinician by the comparison of the loudness of the second sound as heard at the base of the heart and under the aortic cartilage, the relative intensity in the former position increasing in some proportion with tension in the pulmonary artery. But the loudness of the pulmonary element of the second sound is greatly modified by con-

ditions not directly affecting arterial tension, such as the conducting power of the interposed lung and proximity of the artery to the chest-wall. The presence or absence of reduplication, supposing the first sound to be single, is determined by arterial tension alone. In conclusion, there seems reason to believe that we have in the study of the second sound of the heart an opportunity of estimating, as can be done in no other way, the tension of the blood in the pulmonary artery, and hence the activity of the circulation in the lungs and the completeness with which the vital process of oxidation is carried on. In this estimate must be included as factors the consideration of other variables, namely, the height of systemic arterial blood-pressure, as judged from the tension of the radial pulse; the condition of the vasomotor system, especially of the splanchnic area; the tone of the skeletal muscles, particularly those of the abdominal wall; and, finally, the condition of the ventricles of the heart as regards the efficiency of their contraction, and the presence or absence of the signs of asynchronism in the action of the two sides.

SUMMARY AND CONCLUSIONS. Reduplication of the first sound of the heart is a frequent phenomenon, especially in pathological conditions. It may have every degree of completeness from mere prolongation of the first sound to distinct doubling of the same. The condition is most marked at the end of expiration.

Reduplications of the first sound may have various causes, but may be grouped under two heads, as *real* or *simulated*. Under the first division fall those reduplications of the first sound due to asynchronism in the contraction of the ventricles.

There is also reason for the suspicion that reduplication may have its origin in a double systolic effort of the ventricles.

Simulated reduplication of the first sound is probably frequently caused by undue lack of synchronism between the contraction of the ventricle and the tension-sound of the corresponding auriculo-ventricular valve. Simulated reduplication may arise from a post-systolic blow of the pulmonary artery against the chest-wall.

Simulated reduplication of the first sound may be due to audibility of the auricular contraction. No doubt other physiological or adventitious conditions may cause apparent doubling of the first sound.

The prominent factor in causing real reduplication of the first sound is intra- and extra-ventricular blood-pressure. As a rule, that ventricle contracts first within which the diastolic blood-pressure is relatively increased.

When reduplication of the first sound is perceived in normal subjects, it often indicates a lack of cardiac co-ordination, which provokes special symptoms referable to the circulation.

True reduplication of the second sound of the heart is produced by asynchronous tension of the two sets of sigmoid valves.

The phenomenon is a normal one, the aortic valve tension preceding the pulmonary at the end of inspiration and beginning of expiration.

The splitting of the second sound may be wholly absent or only perceptible at about the end of inspiration, or reduplication may be represented by a double sound throughout the respiratory cycle.

The widest reduplication of the second sound occurs when the ventricles are asynchronous in action. When the right ventricle slightly precedes the left the second sound is single, and, conversely, when the second sound is single the contraction of the ventricles is usually asynchronous.

When the first sound is single the character of the second sound as regards reduplication depends upon the ratio of pulmonic to systemic arterial blood-pressure. The greater the difference between these pressures the more marked the reduplication, and *vice versa*. Therefore, when the lung vessels are congested or resistance to outflow from them is increased, reduplication of the second sound is diminished or absent. At the beginning of fevers a single second accompanied by a double first sound has been found; the reverse condition follows as convalescence is reached.

True reduplication of the second sound is heard most plainly at the base of the heart under the second and third left costal cartilages bordering upon the sternum.

Position of the body and especially respiratory movement influence reduplication of the second sound, in so far as they influence the ratio of pulmonic to systemic arterial pressure.

There is reason to believe that the maximum difference between aortic and pulmonary arterial pressures is rhythmically reached at the end of inspiration and the beginning of expiration—that is, in the phase of respiration in which the splitting of the second sound is most marked.

We are probably now in possession of sufficient physiological data to make the estimate of the conditions involving reduplication of the heart-sounds of considerable clinical value.

A CASE OF TUBERCULOSIS OF THE BREAST,

WITH AN ANALYSIS OF ALL CASES OF TUBERCULOSIS OF THE BREAST RECORDED IN MEDICAL LITERATURE.

By CHARLES L. SCUDDER, M.D.,

SURGEON TO THE MASSACHUSETTS GENERAL HOSPITAL, OUT-PATIENT DEPARTMENT; ASSISTANT IN CLINICAL AND OPERATIVE SURGERY, HARVARD UNIVERSITY, BOSTON, MASS.

AMONG the fifty cases of tumor of the breast which came to my clinic at the Massachusetts General Hospital, Surgical Out-patient Department, during the last service, there appeared:

Mrs. Y., an Italian, aged forty-three years. She has had seven children. The eldest child is twenty-five, the youngest child is three years. She has always had fairly good health, and remembers no personal illness. Five years ago there was a painful swelling in the left breast, which was opened about one year later. Three years ago, when nursing her last child, there was a return of pain, and a swelling appeared, which was opened. She complains now of pain and persistently discharging sinuses in the breast. Her chief complaint is constant pain.

The physical examination finds a mitral murmur at the apex of the heart. The left breast presents several cicatrices about the edge of the areola, in which cicatrices are seen the openings of sinuses discharging a dirty-white material. No milk comes from the breast. There is felt a small, tender, fluctuating area the size of a large bean near the areola, and there are also areas of induration about the sinuses. The remainder of the breast-tissue feels normal. One or two axillary glands are felt upon this side.

A diagnosis of tuberculosis of the breast was made from the clinical picture, and she was referred to the hospital, where Dr. John Homans, into whose service she went, operated, removing the portion of the breast involved.

The following is the microscopical report of the Pathologist to the hospital:

PATHOLOGICAL LABORATORY,
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

Areas made up of epithelial cells, with here and there giant-cells, and marked infiltration with polynuclear leucocytes. The areas are seen in process of breaking down. Tuberculosis.

J. H. WRIGHT, M.D.

There is no organ or tissue in the body which is free from the ravages of tubercular disease. Even the mammary gland is occasionally the seat of tuberculosis.

Anatomical and bacteriological evidence must determine whether any case under consideration is one of tuberculosis or not.

It is upon this basis that the cases reported have been judged and have been accepted or rejected as tubercular.

The microscopical evidences of tuberculosis are the finding of either the tubercle bacilli or the anatomical tubercle, or both together, in the diseased tissues or in the discharges from these tissues through a fistulous opening or through the nipple. To determine that a given case is one of primary or secondary infection, through either metastasis or contiguity of tissue, is far more difficult and in many instances is well-nigh impossible, without a complete autopsy.

Many cases of chronic mastitis, chronic abscess of the breast, mammary fistulæ, and scrofulous tumor, so-called, are the results of tubercular infection. Cases have been reported which clinically were tubercular, but in the absence of positive evidence they have been rejected.

A very careful search of medical literature finds, including the case

above reported, but 80 instances recorded as tuberculosis of the breast. Twenty-three of the 80 cases are lacking in positive anatomical and bacteriological evidence and are not to be regarded strictly as tubercular.

Four of the 80 cases are *distinctly secondary, viz.:*

Case 9 (Mandry) was secondary to ostitis of the rib.
Case 12 (Mandry) was secondary to axillary glandular enlargement.
Case 18 (Müller) was secondary to axillary glandular enlargement.
Case 25 (Gaudier and Peraire) was secondary to caries of the sternum.

These four and the remaining fifty-three cases are the only reported instances of tuberculosis of the breast in medical literature.

A list of these cases and the surgeons reporting them, together with the references to literature, are here given.

Fifty-three Cases of Tuberculosis of the Breast.

Case 1. Rémy et Noel. *Bulletin de la Soc. anatomique*, June 1893, p 412.
Case 2. Walther et Pilliet. *Bull. de la Soc. anatomique*, April, 1895, p. 312.
Case 3. Powers. *Annals of Surgery*, 1894, p. 159.
Case 4. Powers. *Annals of Surgery*, 1897, p. 86.
Case 5. Villar. *Gazette des Hôpitaux*, 1894, p. 606.
Case 6. Le Dentu. *Revue de Chirurgie*, 1881, tome i, p 27.
Case 7. Lotheissen. *Wiener klinische Wochenschrift*, 1897, No. 34, p. 763.
Case 8. Mandry (Habermaas). *Beiträge zur klinischen Chirurgie*, 1891–2, vol. viii. p. 179.
Cases 10, 11, 13, and 14. Mandry. *Ibid.*
Case 20. Poirier. *Thèse de Paris*, 1883.
Case 21. Hebb. *Trans. Patholog. Soc.*, vol xliv. p. 123. London.
Case 22. Schede. *Deutsche medicinische Wochenschrift*, 1893, p. 1316.
Case 24. Reerink. *Beiträge zur klinischen Chirurgie*, 1895, vol. xiii. p. 49.
Case 27. Gaudier and Peraire. 1st and 3d Case. *Ibid.*
Case 28. Sabrazez and Binaud. *Archives de Médecine experim.*, 1894, No. 6, p. 838.
Case 29. Demme. Schmidt quotes from 26th Bericht über die Thätigheit des Jennerschen Spitals. Bern, 1889.
Case 30. Ugo Pisani. *Policlinico*, 1896, vol. iii. No. 23, p. 594.
Cases 33 and 35, Bender, 1st and 3d. *Beiträge zür kl. Chirurgie*, 1891–2, vol. viii. S. 205.
Case 36. Habermaas. *Beiträge zur kl. Chirurgie*, 1886, Bd. ii. (quoted by Bartels).
Case 39. Johannet. *Revue Médico-chirurgicale*, tome xiii., 1853.
Case 42. Richet. *Gazette des Hôpitaux*, No. 55.
Case 43. Duret. *Le Progrès Médicale.* Paris, 1882, No. 9.
Case 47. Dubar. *Des Tubercules de la mamelle. Thèse.* Paris, 1881.
Cases 48 and 49. Ohnacker. *Archiv für klin. Chirurg.*, Bd. 28.
Cases 50 and 51. Orthman. *Virch. Archiv*, Bd. 100.
Case 52. Kramer. *Centralb. für Chirurg.*, vol. xv. Zeit. p. 867.
Cases 53 and 54. Piskacek, 1st and 2d. *Med. Jahrbücher.* Wien, 1887, S. A.
Case 59 Piskacek, 7th. *Wien. med. Jahrbücher*, 1887, Bd. 10.
Cases 62 and 65. Berchtold. *Ueber Mammatuberkulose*, 1880. Uster, quoted by Mandry.
Case 66. Berchtold. *Ueber Mammatuberkulose*, 1890. Uster.
Case 68. Hering. *Inaugural Dissertat. Erlangen*, 1889. Mandry.
Cases 69 and 70. Roux. *De la Tuberculose Mammaire.* Genève, 1891.
Cases 71 and 72. Dubreuil. *Gazette Médicale*, April 28, 1888.

Case 73. Shattock. *Trans. Path. Society.* London, 1889, vol. xl. p. 391.
Case 74. Souplet. *Bulletin Société Anatomique.* Paris, 1886.
Cases 75 and 76. Reverdin. Quoted by Bartels, without reference.
Case 78. Bartels. *Inaug. Dissert.* Marburg, 1892.
Case 79. Ely. *Proceedings of New York Path. Soc.*, 1891, p. 81. (Quoted by Powers.)
Case 80. Scudder. Writer's case here reported.
Case 81. Dubar. *Des Tuberculoses de la mamelle. Thèse.* Paris, 1881.
Case 82. Davis. *Medical News*, Philadelphia, June 12, 1897.
Case 83. Davis. *Ibid.*

The references to the four cases of evident secondary tuberculosis of the breast are:

Case 9. Mandry (Habermaas). *Beiträge zur klinischen Chirurgie*, 1891–2, vol. viii. p. 179.
Case 12. Mandry. *Ibid.*
Case 18. Müller, Ludwig. *Inaugural Dissertation.* Würzburg, 1893.
Case 25. Gaudier et Peraire. *Revue de Chirurgie*, 1895, vol. xv. p. 768. A fourth case.

There were 23 cases reported as tuberculosis of the breast which were rejected because of insufficient proof. A list of these rejected cases follows:

Cases 15 and 16. Billroth. *Deutsche Chirurgie*, Billroth u. Lücke, published 1880. (Quoted by Le Dentu, *Rev. de Chir.*, 1881, p. 27.)
Case 17. Park. *Medical News*, vol. lxix. 1896, p. 524.
Case 19. Horteloup. *Tumeurs du Sein chez l'homme.* Paris, 1892. (Quoted by Poirier, Thèse de Paris, 1883.)
Case 23. Schede. *Deutsche medicinische Wochenschrift*, 1893, p. 1316.
Case 31. Lane. *British Medical Journal*, 1890, vol. ii. p. 630.
Case 32. Lane. *Transactions of Clinical Soc.*, 1892, vol. xxv. p. 243.
Case 34. Bender. *Beiträge zur kl. Chirurgie*, 1891–92, vol. viii. S. 205.
Cases 37 and 38. Velpeau. *Maladies du Sein*, 1854, cited by Bartels.
Case 40. Heyfelder. *Deutsche Klinik*, 1851, No. 48.
Case 41. Richet. *Gazette des Hôpitaux*, No. 55.
Case 44. Duret by Lotheissen. *Le Progrès Médicale.* Paris, 1882, No. 9.
Case 45. Duret, same with Case 43. *Le Progrès Médicale.* Paris, 1882, No. 9.
Case 46. Duret, same with Case 44. *Le Progrès Médicale.* Paris, 1882, No. 9.
Case 55. Piscacek. *Wien. med. Jahrbücher*, 1887, Bd. 10.
Cases 56, 57, 58, and 60. Piscacek. *Wien. med. Jahrbücher*, 1887, Bd. 10.
Cases 61, 63, 64. Berchtold. *Ueber Mammatuberkulose*, 1890. Uster, Bartels.
Case 67. Hebb. *Trans. of Patholog. Society*, 1888. London.
Case 77. Kummer, quoted by Bartels. *Inaug. Diss.* Marburg, 1892. No reference given.

It is necessary to make brief mention of the 23 rejected cases. In the sputum of several cases of Piscacek, namely, Cases 55, 56, and 58, tubercle bacilli were found. The individuals had tuberculosis of the lungs and presented, clinically, tubercular lesions in the breast. It would be highly improbable that in manifestly tubercular subjects, in whose sputa tubercle bacilli were found, lesions in the mammary gland clinically resembling those of tuberculosis should be any other than tubercular.

Billroth, two cases: one, Case 15, presented multiple cheesy nodules which healed after incision and cauterization; the second, Case 16, presenting nodules in the breast, some of which contained cheesy material, died of tuberculosis.

Horteloup's case (19) presented a flattened tumor about the nipple, with tuberculosis of the lungs and of the epididymis.

Schede's second case (23) was a pathological specimen, incompletely recorded; no history was reported.

Of Lane's two cases, one (Case 31) showed abscesses in the breast and caseous lymphatic glands; the other (Case 32), in a phthisical subject, presented a breast abscess.

Bender's case (34), in a phthisical subject, showed both breasts involved with a hard tumor fluctuating in one spot and with enlarged axillary glands.

Velpeau's two cases (37 and 38) presented hard, lumpy feeling masses, one fluctuating, the other having fistulæ.

Heyfelder's case (40) was that of a large abscess near and overlapping the region of the breast, acute in its course.

Richet's case (41), in a phthisical subject, was a cold abscess in the breast with enlarged axillary glands.

Duret's case (44), reported by Lotheisen, is probably the same as Case 46, in which there was an axillary swelling the size of a small apple, tender and movable, together with cheesy glands.

Duret's case (45) is the duplicate of Case 43, which is accepted.

Piskacek's case (55) is a phthisical subject in whose sputum tubercle bacilli were found. The left breast was atrophic, very little glandular tissue was present. There were scars in the skin of old fistulæ, and there were existing fistulæ. There was an ulcer near the nipple, with violet-colored edges. Clinically, this would seem to be a very satisfactory case.

Piskacek's case (57) exhibited fistulæ following a mastitis, and Case 60 exhibited a hard swelling of the right breast, softening in places, an ulcer of the skin and fistulæ.

Berchtold's case (61) was an individual presenting glands in the neck and multiple hard nodes in the breast, which had softened, discharged, and healed.

Berchtold's case (63) was a girl, aged fifteen years, who had had no catamenial period. A fluctuating swelling the size of a fist was opened and curetted.

Berchtold's case (64) was an individual with phthisis and an old pleurisy, who had a hard, tender swelling in the right breast and an axillary abscess in the right axilla.

Hebb's case (67) was a woman, aged thirty-nine years, who had had hæmoptysis. She had had eight children, five of whom had died of

consumption. She presented a hard, movable tumor in the breast, and the lymphatics were enlarged to the axilla.

Kummer's case (77) was a child, aged sixteen years, with an axillary swelling extending toward the breast. An abscess had opened under the nipple. The sinus healed. Other abscesses opened. Fistulæ were present. The axillary glands were enlarged.

Methods of Infection. In primary mammary tuberculosis the tubercle bacillus must find its way into the organ through the milk-ducts or through an open wound of the nipple, as in Case 29 (Demme), or of the skin over the breast. If the primary infection is through the milk-ducts, the glandular acini will be first involved; if infection be through the wound of the skin, the interstitial tissue is first attacked.

Metastatic mammary tuberculosis or autoinfection, in which the infectious agent obtains access to the breast through the vascular channels from a tubercular focus situated in some distant portion of the body, is the most common form.

As a secondary disease through contiguity of structure, tuberculosis of the breast may follow caries of the rib or sternum, empyema of the chest, and tuberculosis of the axillary and neighboring lymphatic glands.

Hereditary Influences. Tuberculosis is not hereditary, but there still exists a well-founded notion based upon experience that a lack of resistance in the tissues to tuberculous infection is inherited.

Case 4 (Powers) had two sisters and a brother who died of phthisis. Case 10 (Mandry) and Case 28 (Sabrazes and Binaud) each had a tubercular family history. Case 29 (Demme), Case 48 (Ohnacker), Cases 53 and 54 (Piskacek), Cases 62 and 65 (Berchtold), and Case 78 (Bartels) all presented a tubercular history in the immediate family.

The existence of tuberculosis in the immediate family of any patient must be given its due weight in doubtful cases of breast tumor.

The Age. The majority of all the cases were thirty-five years old or younger. A number were under twenty years of age. The oldest case recorded was but fifty-three years. Mammary tuberculosis occurs in comparatively young adults—*i. e.*, during the period of functional activity of the gland.

Additional Tubercular Foci. In many cases the facies of the patient was evidently tubercular. The well-recognized "scrofulous" diathesis was present, and, in addition, tubercular infection already existed in many different tissues remote from the mammary gland, the breast lesion being only one of two tubercular lesions in the same individual. The lymphatic glands of the neck, the bones of the elbow-joint, of the sternum and the ribs, the apices of the lungs, the epididymis, the sacro-iliac synchondrosis, the pleura, and the peritoneum, all manifested tubercular lesions.

PREVIOUS CONDITION OF THE BREAST. About half the cases had borne children, and the breasts of these women had been functionally active. About ten of the cases were reported to have had an inflammation of the breast at some time previous to the appearance of the tubercular infection.

Lactation was active during the development of the tubercular disease only a few times. Does an inflammation of the breast during the puerperal period predispose to a tuberculosis of the breast? In a series of 17,999 well-observed cases at the Boston Lying-in Hospital,[1] there were 92 cases of abscess of the breast. This is a low percentage of one-half of one per cent. It is not known, of course, that all these cases were free from tuberculosis.

In the cases here recorded there is over 13 per cent. of mastitis; that is, in the tubercular puerperal cases there is a greater frequency of abscess than in the normal puerperal cases. It may be that the tubercular infection finds a soil more favorable to its development in a breast once the seat of an inflammatory process. The percentage at the Boston Lying-in Hospital must not be taken as expressing the frequency of mastitis, for these cases are under observation there but a short time, and may develop after that period.

Inoculation experiments were successful in nine of the reported cases. Intraperitoneal inoculation of guinea-pigs was done in all but one case, in which inoculation intc the eye of a rabbit was successfully tried.

Series of Cases in which Inoculation Experiments were made Successfully.

Case 5. Villar.
Cases 25, 26, and 27. Gaudier and Peraire.
Case 28. Sabrazes and Binaud.
Case 30. Ugo Pisani.
Case 49. Ohnacker.
Case 62. Berchtold.
Case 65. Berchtold.

In 3 of the 9 cases in which the inoculation was positive, no bacilli were discovered in the abscesses or breast tumor.

It is merely an interesting fact, in passing, to note that 4 of the tuberculous cases were men, and that 2 of the rejected cases were also men. These are the male cases of the accepted list:

Case 20. Porier.
Case 21. Hebb.
Case 22. Schede.
Case 29. Demme.

These are the 2 male cases of the rejected list:

Case 19. Horteloupe.
Case 40. Heyfelder.

[1] These statistics were furnished through the courtesy of Dr. Edward Reynolds, Boston Lying-in Hospital.

SUBJECTIVE EVIDENCES OF THE DISEASE. In about half of the cases reported *pain* in the breast is mentioned as an early and constant sign. In a few cases the pain was stated as severe. In the case reported by the writer, in which there was no acute inflammatory process at the time examined, the patient came seeking relief not so much from the discharging fistula as from the persistent pain in the breast.

In a large number of cases the disease is discovered by the patient when already well established. It offers no warning and proceeds in a quiet and peculiarly stealthy fashion.

The breast itself, often small and insignificant in advanced cases, at the beginning of the disease may be found enlarged, independently of the presence of an abscess or definitely defined tumor. This enlargement is due to the very great round-cell infiltration, giving an indurated, brawny feel to the part of the breast involved.

The nipple was retracted in only a few of the cases reported.

The tubercular process has appeared in the breast in variable forms, from a single small node or many nodules, firm in consistency, resembling lymph glands, seated in the periphery or scattered through the breast, to a hard, irregular, ill-defined lumpy mass the size of an orange in the centre of the breast gland. There are many gradations. These masses may be movable in or fixed to the breast gland. They may be immovably fixed to the pectoral fascia. The skin over these masses is usually unattached. These masses may extend well outside the mammary gland toward and even to and into the axilla of the same side.

As the tubercular process progresses these masses become somewhat less well-defined, their outlines are more indistinct; they seem attached to the contiguous tissues. There is a doughy, indefinable feel upon palpation. Still later in the evolution of the tubercular process, here and there throughout the presenting tumor, there is a softness felt; fluctuation is present. The skin is attached to some part of the softened area, the skin becomes red, ulcerates, and through the resulting sinus appears a discharge of pus and of a puriform caseous material.

It is interesting that in the majority of instances the masses in the breast which softened first did so near to the nipple. If suppuration in tubercular lesions necessitates the introduction of an infectious agent other than the tubercle bacillus, it would seem that the nipple afforded an easy entrance to the pyogenic coccus.

THE PROGRESS OF THE DISEASE. The tubercular process was characteristically a slow one in almost all instances. It occupied months and even years in its course from the time it was first noticed by the patient to the time that the disease was examined by the physician.

In the writer's case five years was the duration of the disease. Mandry (Case 14) reports a case of four years' duration.

In the following four cases the course of the disease is reported as

having been very rapid: Case 9, Habermaas (by Mandry). Case 12, Mandry. Case 21, Hebb. Case 31, Lane.

Case 31 was not proved to be tubercular. Cases 9, 12, and 21 may have had a secondary infection, therefore the rapidity of their progress.

FISTULA. In more than half the cases a fistula was present. A few cases showed fistulæ in the axilla. Multiple fistulæ were found in several instances. The openings of the fistulous tracts appear as ulcers with undermined bluish edges filled with pale, flabby granulations from which a thin puriform caseous discharge proceeds.

AXILLARY LYMPHATICS. In nearly all cases the axillary glands presented different stages of tuberculosis. They were at times hard or softened, small or large, and fistulæ were present from these axillary glands with the characteristic openings.

In so many instances the enlargement of the glands of the axilla preceded the manifestation of the disease in the breast that it is reasonable to suppose that it was primary in the axilla. This was very evident in Case 75 (Reverdin).

CAUSES OF DEATH. Few cases have been followed carefully until death.

In those reported as having died, Case 3 (Powers) died of phthisis four years later. Case 8 (Habermaas, quoted by Mandry) died of tubercular peritonitis. Case 16 (Billroth) died of tuberculosis, presumably miliary. Case 51 (Orthmann) died of tubercular pleurisy and pericarditis.

TUBERCLE BACILLI. In 29 cases the tubercle bacilli were found. Ugo Pisani reports them in the pus from the abscess. Orthmann reports them as in the axillary glands. Piskacek reports them as in the pus of fistulæ. Roux and Hering report them as in the mammary gland and the axillary glands. Davis reports them as found, in his first case, in the tissues. *Microscopically*, the reported cases show the anatomical tubercle with characteristic giant-cells in the axillary glands, in the walls of abscess-cavities, in the acini of glands, in the walls of fistulæ, and in the new connective tissue. In a few instances macroscopic miliary tubercles were seen. In all instances the round-cell infiltration is very great. The breast tissue is found cirrhotic and often has nearly disappeared. The bloodvessels show an endarteritis. In many cases the bloodvessels are few in number (Bender and Poirier). The pectoral fascia and muscle are found involved in the tubercular process. From the evidence of the reported cases, carefully considered, it would seem highly probable that the occurrence of a purely primary tuberculosis of the mammary gland is extremely rare.

The so-called case of primary tuberculosis is secondary to a tubercular lesion in some other part of the body, if not due to contiguity of tuberculous tissue.

Spediacci, *Schmidt's Jahrb.*, vol. ccxlvii., p. 148, 1895, from his experiments with the inoculation of guinea-pigs and rabbits, suggests that all tuberculosis of the mammary gland is secondary.

DIAGNOSIS. From the ordinary *pyogenic infections* tuberculosis may be distinguished by the absence of a sudden onset and acute inflammatory symptoms.

When the breast tumor is hard or firm other solid tumors must be considered, and the diagnosis is often difficult. From *carcinoma* of the breast tuberculosis is distinguished by the less isolated and softer feel of tuberculosis; tuberculosis occurs in younger patients; the axillary glands of tubercular subjects are involved early; in carcinoma the axillary glands are usually enlarged late in the disease. The firmness or extreme hardness of carcinoma is very characteristic; tuberculosis very rarely attains such board-like hardness. If present, the cachexia of the two diseases is very different. The clinical picture of tuberculosis is quite different in its details from that of carcinoma.

The *gummata of syphilis* may be distinguished from tuberculosis by the specific history and the positive results of antisyphilitic treatment.

After softening of the tubercular tumor, whether in whole or in part, the diagnosis is attended with less difficulty. *Actinomycosis* of the breast is to be distinguished from a tubercular cold abscess and chronic fistulæ. The discovery of the actinomyces by the gross and microscopical appearances will make the diagnosis certain.

From *cysts* of the breast, the fluctuating tubercular tumors may easily be differentiated in that the breast-cysts are usually tense and firm. There is no inflammatory exudate about the breast-cysts, so that they are clearly defined, whereas the fluctuating swellings of tuberculosis are softer and often ill-defined.

As a help to diagnosis, Roswell Park[1] suggests that the discharge from the fistulous tract, the fluid from the fluctuating swelling, should be examined microscopically; if tubercular, it will show a lack of the granular débris and formed elements. The same discharge should be stained for tubercle bacilli. A guinea-pig should be inoculated with the suspected fluid. The inoculation-test will be final and satisfactory even when the microscopical examination proves to be negative. A bit of solid tissue may be removed and examined histologically and may be used for inoculation experiments. It is of value in this connection that in a case reported by Davis (82) tubercle bacilli were found in the discharge from the nipple previous to operation.

PROGNOSIS. The prognosis as to local recurrence and complete recovery after thorough removal of the breast and axilla and all glands is, of course, dubious in distinctly tubercular subjects and those in

[1] Surgery, by American Authors.

whom the mammary lesion is evidently due to auto-infection. On the other hand, in apparently healthy subjects, with few or small axillary glands (the disease appearing to be primary in the breast), the prognosis both as to local conditions and complete recovery of health is excellent.

TREATMENT. The following have been the methods of treatment in the reported cases:

1. Curetting of sinuses.
2. Cauterization of sinuses.
3. Removal of the tumor from the breast.
4. Removal of the breast and the tumor.
5. Removal of the axillary glands.
6. Removal of the breast and axillary glands.

Complete removal of all disease, including the whole breast and all the glandular contents of the axilla, is the only thorough treatment advisable.

It is possible to imagine a tubercular focus lying isolated in the breast-tissue which can be removed completely without sacrificing the gland itself. Practical experience proves, however, that partial operations are dangerous.

The old method of curetting tubercular abscesses and chronic fistulæ of the breast, in the hope of their healing, has been discarded. A better understanding of the pathological conditions present in the abscess-wall has changed this treatment to radical excision of all the disease with a wide margin. The wide margin is necessary, for tuberculosis extends further into surrounding tissues than can be seen with the naked eye.

In addition to operative procedure, the general constitutional and climatic treatment should be followed as in cases of tuberculosis in other parts of the body.

189 BEACON STREET, BOSTON, MASS.

REVIEWS.

DISEASES OF THE STOMACH: Their Special Pathology, Diagnosis, and Treatment, with Sections on Anatomy, Physiology, Analysis of Stomach Contents, Dietetics, Surgery of the Stomach, etc. In three parts. Pp. 788. By JOHN C. HEMMETER, M.B., M.D., Ph.D. Philadelphia: P. Blakiston, Son & Co., 1897.

THIS work of three parts is consolidated into a single bulky volume of 788 pages The book is unique in that it is by far the most voluminous single volume treatise on the subject published, and that apart from the small volume of Einhorn's (really a collection of monographs) it is —although perhaps not the first projected—the first American treatise on diseases of the stomach to appear.

Part First is devoted to the anatomy and physiology of the digestive organs, including a description of "Methods and Technics of Diagnosis." Part Second treats of the "Therapy and Materia Medica of Stomach Diseases." Part Third is termed "The Gastric Clinic," and concerns itself with the study of the different diseases of the stomach.

The author, although a comparatively recent laborer in this field, has, by virtue of natural ability, great industry, and marked enthusiasm, aided by certain other favorable conditions, accomplished a considerable amount of most admirable work which has formed the basis of his treatise. His enthusiasm in his specialty is unbounded; evidences of that are apparent from the outset, as in the preface, in which is evinced a self-satisfaction with his creation most commendable. This enthusiasm is only unfortunate in that it sometimes has led to the display of a trifle too much of the Ego, as it has to the origin, advocacy, and voluminous description of certain methods of research, which, although most commendable, are often impracticable of application by the general practitioner, for whom it is stated the book is intended.

At the start we cannot but enter a protest against the term "gastro-enterologist," often employed by the author in seemingly the sense that diseases of the digestive apparatus should be regarded as forming a distinct specialty, as is that of diseases of the eye and ear, the nose and throat; these being so often entered into without a preliminary thorough training in internal medicine. We cannot but feel sorrow for those falling into the hands of such specialists as may require the caution Dr. Hemmeter has seen fit to give on page 370: "Gastro-enterologists should not fail to perfect themselves in the technic of auscultation and percussion!" If those working in this line have not first had ample preliminary training in auscultation and percussion, and subsequent thorough application of these in hospital and private work, before they have turned their attention to a branch so intimately related to the broad field of internal medicine as not to be separated from it, they

should be posted as charlatans, and deprived of the power to practise on suffering humanity. But we feel sure that it is not to such of these that Dr. Hemmeter has meant to appeal, although a caution to such in the book would not have been inappropriate.

It seems a trifle needless to quarrel over the question of priority of introducing a tube into the duodenum (p. 669), or the gastro-diaphane into the colon (p. 103). Certain claims to priority of this sort, however just, are urged somewhat obtrusively, as if one might suppose such a procedure were patented and the danger of infringement of the same imminent. Concerning the claim of priority of illuminating the colon (p. 103), it must be remarked that it is unfounded, since in the published work of Heryng and Reichmann, on gastro-diaphany (*Therapeutische Monatshefte*, March, 1892), who had interested themselves in this subject since 1889, there is graphically illustrated the diagnostic value of transillumination of the colon. Their work was done with a water-circulating diaphane, an apparatus far safer for such exploration than that employed by Dr. Hemmeter. Dr. Hemmeter may, however, justly claim not only priority but, we think, isolation, when the question of introducing the diaphane into the ileum (!) is concerned. Concerning the use of the gastro-diaphane, by the way, we think the author has not dwelt sufficiently upon the sources of error in its application, such as occur through too great diffusion of the light, so liable to occur when lamps of high illuminating power are employed. It seems odd that mention is not made of the most admirable water-circulating diaphane, which possesses material advantages over the original apparatus of Einhorn, as the reviewer can testify. It certainly is the form that should be used with lamps of such high voltage as Dr. Hemmeter employs. This is especially true when illumination of the bowel is the object.

Dr. Hemmeter has shown a tendency to a little diffuseness leading occasionally to undue repetition. A commendable desire for prompt publication is doubtless the cause of any such blemish, as it is of certain defects in style and English here and there somewhat apparent. We cannot but say that we feel that it would have been better for publisher and author if the book had been a little less voluminous. We think that, with other matter that might have been curtailed, considerable in the chapters on Dietetics and the Diet Kitchen could have been omitted, as might also the introduction of expensive plates (tending naturally to increase the price of the book) illustrating the working of the author's kymograph in his description of ascertaining the condition of the gastric peristole—a method which, by the way, is scarcely practicable for general clinical employment. The reproduction of Fig. 21 (p. 131) as Fig. 40 (p. 716), and of Fig. 22 (p. 133) as Fig. 34 p. (428), seem unnecessary, from the undue amount of space thus consumed. In the effort not to omit an extensive bibliographic reference, authors' names and titles, and often title of publication and date, are repeated both in the text and at the close of the chapter. Concerning somewhat careless or little polished use of English here and there apparent, there may be incidentally pointed out the following: "Apparatuses" (p. 78), "digestive clinical pathologist" (preface). Figs. 21 and 40 are described as "from a case of persistent hyperacidity found in the eye of the tube." On page 139 the following occurs: "We have seen a number of cases whose stomachs were of natural size and where there was no disturbance, ..." On page 274 it is remarked that "the use of

alcohol in any shape is totally unnecessary for the use of the human organism." "Potassium iodide may lead up to gastritis" (p. 395). A tendency to an unsightly mixture of English and Latin is a direction on p. 450: "ʒss in ℥ij aqua after meals." The "of water" would appear to better advantage in English. By "Bruce Jones" (pp. 382, 383) is probably meant Bence Jones.

More important of attention and correction are occasional slight errors in another direction: "alcohol free ether is as totally unnecessary for use in the application of the Uffelmann test to separate the lactic acid in the gastric filtrate as it is essential for employment with the aldehyde method proposed by Boas" (pp. 152, 153). Alcohol free ether is advised for use in the first and merely "ether" with the second. Toepfer's test is spoken of as one for free HCl alone (p. 148), whereas it also responds to the loosely bound HCl, to which the phloroglucin-vanillin gives no reaction. As concerns the occurrence of a rose-color reaction with the latter as an indication of the presence of traces of the mineral acids alone, it may be of interest here to record that the reviewer long ago showed that boric acid also gives a rose-hue response macroscopically identical with the reaction obtained from traces of a mineral acid. On page 669 one grain of salol evidently should read one gramme.

The directions concerning the application of lavage and the single and double gastric tube are, we think, scarcely given as minutely as the importance of the subject warrants. A thorough knowledge of the technique of the various diagnostic methods is of little utility without an exact comprehension of the needs and best modes of use of a remedy often so badly applied as to be useless or harmful. More space could have been devoted to describing the great value of douching in comparison with mere washing of the stomach, and as to the utility of other double-current spray tubes than those described. Einhorn's intra-gastric spray, which is unqualifiedly commended, will be often found to be impracticable through its introducing so much air into the stomach. Surely it is not intended that a 6 per cent. solution of HCl should be employed for lavage (p. 321). This would be effective enough in overcoming "decided fermentations," but would be hard on the stomach.

The statement (p. 377) that there is usually present in gastric carcinoma, as in malignant disease elsewhere, a constant increase in the number of leucocytes, varying from 10,000 to 50,000, is somewhat misleading. A leucocytosis, as concerns decided numerical increase, is not regarded as relatively very frequent in cancer of the stomach, and a marked grade of leucocytosis before extensive metastasis has occurred is unusual.

We are surprised to note that ergot is said to be of utility in "copious and persistent" gastric hemorrhage (p. 482). A consideration of the physiological action of ergot, with the repeated failures following its employment, if other measures really efficient are not coincidently used, should soon convince one of its inutility. The writer (see *Medical News*, January 23, 1892, and *System of Practical Therapeutics*, vol. ii. p. 949), so convinced several years ago, never nowadays employs it in gastric hemorrhage.

On page 526 is recommended, as an aid to secure particles of the growth in gastric carcinoma, the employment of a stomach-tube which "although quite soft is provided with a sharp chisel-like edge around

the lower opening." Such a tube to be of utility as a curette, it should be needless to say, would be dangerous of application. We think that the author lays far too much stress on the diagnostic value of the discovery in the wash-water, in cases of suspected gastric carcinoma, of isolated cellular elements, whether showing karyokinetic figures and forms of mitosis or not. So, too, if, in the statement (p. 526) "nor should we always deny the existence of cancer when we find no fragments giving the typical histological structure of these neoplasms," *ever* was substituted for "*always*," it would be more exact. We think trained clinicians will not agree with the author that the actually characteristic rose spots of enteric fever ever occur in another disease, not even acute miliary tuberculosis (p. 550).

We think Dr. Hemmeter goes a trifle too far in holding that constipation occurring in chronic gastritis should never be treated by drugs. A mild laxative, such as a reliable preparation of cascara, is sometimes absolutely essential to supplement the agents he advises, as is also an occasional good-sized dose of calomel. The latter has an influence most far-reaching for good on other organs and parts than the stomach, which tend to derangement in this affection. His treatment of chronic gastritis is too much that of the stomach alone. Because extensive fermentation and formation of organic acids are of rare occurrence in this disease, it does not follow that saccharine articles of diet may be always permitted. We must consider the influence of these upon metabolic processes in the liver, as well as upon the intestinal condition.

The author's scepticism concerning the frequency of loose right kidney in women is somewhat remarkable, as is the statement that the rate for Baltimore is but 6 per cent. (!). He remarks that "a surprisingly large number of movable kidneys are diagnosticated by otherwise very skilful diagnosticians when they are really dealing with cases of descent of the liver." This seems indeed severe on these otherwise skilful diagnosticians. He regards, also, as the chief error in diagnosis the much less commonly present furrowed, partially separated portion of the right lobe of the liver. The reviewer has paid special attention to this matter for a number of years, and has examined for these conditions as a matter of routine. He is certain that he cannot be so misled. The percentage in which he encounters a palpable and often very mobile right kidney in his patients is at least 30. Evidently either preconceived notions concerning the infrequency of loose right kidney or the method of examining for it adopted, have prevented Dr. Hemmeter from discovering a condition which must be as common in Baltimore as elsewhere. It is most unlikely that the women of Baltimore, although perhaps superior in certain other respects to their Eastern sisters, are better able to sustain their right kidney in position, and that instead they have a too freely movable liver or the less common tongue-like projection cited. In a subsequent edition Dr. Hemmeter will probably somewhat modify his views of this matter. It is no unusual occurrence with the reviewer to be able to demonstrate a very loose right kidney in cases in which it had been overlooked by diagnosticians presumably skilled in the line of abdominal work who had referred the case for opinion. Not being on the watch for this condition, it had previously been either unsuspected or the method employed for its detection was inefficient. Concerning the question of the rarity of finding a loose kidney post mortem, which is adduced against its frequency in life—Dr. Hemmeter holding that the movability should per-

sist in death—Newman's most rational explanation seems to the reviewer sufficient: that the fatty envelope becoming solidified after death tends to fix a kidney which in life had been freely movable.

Enough has been said in the way of criticism of this—taking it all in all—really admirable book. The few points mentioned adversely are, in comparison with the vast expanse of valuable material, the merest trifles—details not detracting from the worth of a book which can truly be said to represent a monument of earnest intelligent work, reflecting credit on the author's skill as an investigator and compiler in this branch of medicine. We confidently commend it to those working in this special field who desire to be abreast of what is being done, and predict for it popularity and a large sale. Much praise is due the publishers for the most pleasing make-up of the volume. Their part has been truly perfectly done.

D. D. S.

THE PRACTICE OF MASSAGE: ITS PHYSIOLOGICAL EFFECTS AND THERAPEUTIC USES. By A. SYMONS ECCLES, M.B., Member Royal College of Surgeons, England, etc. Second edition; pp. xii. 372. London: Balliere, Tindall & Cox, 1898.

THE first edition of this book was reviewed in this JOURNAL for April, 1896. The present edition is practically a reprint of the first, but under the auspices of another publisher. Although nothing of great importance, so far as concerns massage, has presented itself in the time which has elapsed between the two editions, and for this reason no radical changes should be expected, yet the revision as claimed in the preface ought to have been sufficiently thorough to correct the typographical errors of the first, some of which were alluded to in our previous review. Not only has this not been done, but the objectionable tales denominated histories of patients are retained. The book, in spite of its obvious defects, really is a valuable one for the physician. We regret that opportunity for its improvement has not been accepted.

R. W. W.

PICTORIAL ATLAS OF SKIN DISEASES AND SYPHILITIC AFFECTIONS, IN PHOTO-LITHOCHROME, FROM MODELS IN THE MUSEUM OF THE SAINT LOUIS HOSPITAL, PARIS. With explanatory wood-cuts and text. By E. BESNIER, FOURNIER, TENNESON, HALLOPEAU, DU CASTEL, H. FEULARD, L. JACQUET. Edited and annotated by J. J. PRINGLE. Part XII. London: The Rebman Pub. Co. Philadelphia: W. B. Saunders, 1897.

THE part of this valuable work before us concludes the *Atlas*, which must be regarded as an admirable exposition in color of some of the many beautiful models of the famous Saint Louis Hospital Museum. Some of the diseases represented are rare, while others are common, all of them being well chosen. The drawing and coloring of the plates throughout the work are excellent, and the text is not only explanatory but instructive, in some instances amounting almost to small monographs—as, for example, the article by Fournier on Syphilitic Chancre of the Lip. Part XII. contains Syphilitic Chancre of the Nostril, Lip, and Tongue; Xeroderma Pigmentosum; Impetigo Contagiosa, and Urticaria Pigmentosa.

L. A. D.

PROGRESS

OF

MEDICAL SCIENCE.

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD W. WILCOX, M.D., LL.D.,

PROFESSOR OF MEDICINE AND THERAPEUTICS AT THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL; VISITING PHYSICIAN TO ST. MARK'S HOSPITAL.

The Saponins.—M. G. POUCHET points out that these occur in a very large number of plants under a variety of names, as, digitonin, gratiolin, lychnin, githagin, senegin, cyclamin, smilacin, quillagic and polygalic acids. These, which might better be called sapotoxins, differ much in their therapeutic and toxic properties. The method of preparation also has much to do with their activity: by maceration the plant may yield substances of remarkable toxicity; if isolated by appropriate chemical methods they may be almost inactive. If obtained by the latter method they occur as an amorphous powder, which varies in color from white to yellow, and is first of a sweetish, later of a bitter, styptic and burning taste. They are soluble in all proportions in water, slightly or not at all in alcohol. They may be divided into two groups: (1) Neutral or (2) of acid reaction. The latter are distinguished by their solubility in alcohol and by their marked toxicity. They are all lævogyre, their aqueous solutions form emulsions, and they dissolve without water in such substances as lead sulphide and barium carbonate. Chemically they are glucosides. Physiologically they act upon the heart, more or less, as does digitalin, but they show in addition an intense action upon the medulla, which manifests itself by convulsions and asphyxia, from which the animals experimented upon die. They are poisons to the central nervous system and to the heart. If given by the mouth their action upon the nervous system is *nil*, but they irritate more or less violently the intestinal mucous membrane, and further, they are caustic. When given hypodermatically they determine death of the tissues at the point of injection. The acid varieties given intravenously produce results differing according to the doses. If these are large, death follows in a few seconds, preceded by convulsions and paralysis of the nervous centres. In smaller doses dysenteric manifestations are present (hyperæmia, bloody extravasations, œdema of the wall of the intestine, hyaline thromboses, necrosis of the mucous membranes).

Further, ecchymosis and necrotic patches have been found in the pericardium. Then death occurs after some hours. From small doses symptoms of poisoning come on more slowly, and death from collapse supervenes. There are no intestinal symptoms, but a marked lowering of temperature precedes the fatal issue. They dissolve red blood-corpuscles and cause hæmaturia. If the mucous membrane is healthy they are absorbed with difficulty; if abraded they are likely to give rise to symptoms of poisoning. Repeated applications to the skin produce a painful pustular eruption followed by sloughing. Calling attention to the reputation which senega has among the Indians as a remedy for snake-bite, it is suggested that the saponin contained in the root may be antitoxic to venom, comparable or even identical with the antitoxin contained in Calmette's antivenin. Bretonneau recommended senega for the treatment of various bronchial and pulmonary diseases. It slows the pulse and increases cough and expectoration, but should not be exhibited when the stomach is in bad condition, nor in fever. Nor, indeed, should dentifrices containing saponin be employed unless the gums are healthy. Further, it is believed that many of the symptoms and even the lesions which are common in poisoning from plants containing these substances should be attributed to them.—*Bulletin Général de Thérapeutique*, 1898, 6e liv., p. 193.

Strophanthus in the Treatment of Cardiac Disease.—Dr. H. Jacobaeus makes use of the tincture, reporting nine instances. In under-compensated hearts this remedy can be used for many months without interruption, without producing digestive disturbances. Cumulative effects (so-called) are not so often seen as from digitalis. The method of administration is to commence with daily amounts of twenty drops, gradually increasing to double this amount, and as soon as diuresis and improvement in general and circulatory conditions result, to return gradually to the initial amount.—*Klinisch-Therapeutische Wochenschrift*, 1898, Nos. 11, S. 346; 12, S. 390; 13, S. 430; 14, S. 462.

Are the Fluid Preparations of Digitalis Active when Manufactured into Tablets?—Dr. E. M. Houghton has conducted some very careful experiments upon animals, for in this way can be exactly studied the action upon the various organs. It was developed that the quantity of active constituents in different samples, as shown by physiological examination, varied considerably. The fact that some tablets have been demonstrated to be inert is quite likely due to this variation; the fault then being in the fluid preparation and not in tablets made from it. The general conclusion is that active fluid preparations of digitalis do not lose in activity by being made into tablets, nor do the tablets become less active by keeping, than do other preparations of digitalis.—*Therapeutic Gazette*, 1898, No. 4, p. 217.

The Treatment of Diseases of the Heart.—Dr. R. Douglas Powell, in writing of digitalis, believes that the more common mistake is the prescribing of too large a dose at first, which tends to produce premature arterial contraction and cumulative effects. Then, with the appearance of these physiological symptoms the drug is stopped, and other medicine substituted, until the pulse calls for its administration. In this hap-hazard way the heart is never held in good control. If there is urgent need to push the drug, digi-

talin is best used subcutaneously. In ordinary cases a dose of 10 minims of the tincture every four, or 15 every eight, or 5 minims every waking hour is sufficient. This given, the patient being at rest, it generally takes about three days before the pulse is under control and the urine begins to increase. When decided effects are produced the drug should be steadily continued in doses calculated to maintain its effect. With ordinary watchfulness there is no risk; timely warning of excess is given by the pulse, which, having become slow, begins to exhibit small intermediate beats, and especially a tendency to go in couples. The sickness which comes with the drug is best relieved by an occasional mercurial or a change to digitalin, or a tumblerful of hot water taken occasionally. In some cases it may be necessary to omit the drug altogether.—*British Medical Journal*, 1898, No. 1944, p. 869.

Experimental Thyroidism.—Dr. R. H. Cunningham presents the results of a careful review of the literature and painstaking laboratory work as follows: (1) Absolutely fresh thyroid gland is not poisonous, in the usual sense of the term, when absorbed through the alimentary canal. (2) The symptoms of induced thyroidism are manifestations of an intoxication resulting from the ingestion of decomposed thyroid material. (3) The so-called experimental thyroidism is not specific for the thyroid only, for the ingestion of many substances derived from animal tissues other than the thyroid gland may produce an intoxication strikingly similar in every respect to that of experimental thyroidism. (4) Most, if not all, animal tissues yield substances which, if injected in large quantities directly into the circulation or beneath the skin, will produce an intoxication often very similar to that produced by injections of various substances derived from the fresh thyroid tissue. (5) The effects resulting from the intravascular or subcutaneous injections of aqueous extracts, decoctions, and the concentrated extractives of the thyroid tissues, of the thymus, of muscle, etc., are by no means necessarily indicative of the function and the action of the hypothetical internal secretions of the same tissues during life. (6) The utilization of the fact that ingestion of decomposed thyroid material produces on certain occasions an intoxication with certain symptoms similar to some of those of Graves's disease is not justifiable for the furtherance of the theory that the symptoms of exophthalmic goitre result from an over-production of the thyroid secretion. (7) The results of this investigation lead to the conclusion that the fresh thyroid tissue yields at least probably two substances that are capable of palliating the symptoms of the acute cachexia in totally thyroidless dogs. (8) The thymus tissue also yields one and probably two substances that are equally capable as the thyroid extractives of palliating the acute cachexia of totally thyroidless dogs. (9) Neither of the above substances is an enzyme, nor does either contain iodine. (10) Neither the feeding of minced raw thyroid glands nor the injection of aqueous thyroid extracts, decoctions, and concentrated solutions of the extracted palliative thyroid principles is capable of keeping totally thyroidless dogs alive longer than a few weeks (possibly three weeks). Still less capable are the thyroid preparations containing decomposition products. (11) The presence of one, or usually several, small accessory thyroid bodies which gradually hypertrophy and wholly or partially assume the functions of the excised thyroid lobes, accounts for the occasionally long

survival of thyroidectomized, thyroid-fed young dogs. (12) Totally thyroidless dogs are so quickly overwhelmed by the cachexia, and the intervals between the thyroidectomy and the onset of severe dyspnœic attacks and the subsequent death differ so slightly, no matter which of the usual varieties of fresh food are employed, that various kinds of fresh food cannot be unquestionably affirmed to influence the onset of the cachexia in any especially definite manner. Animal foods, in which constituents poisonous to rabbits have developed, probably slightly hasten the onset of the severer symptoms, and the vaunted remarkably modifying influence of a diet of ordinary milk does not exist in the case of the totally thyroidless dog. (13) Monkeys, whose general metabolism is disturbed in consequence of the removal of a greater portion of the thyroid gland, evidently become more susceptible to those constituents of meat that are poisonous to rabbits; and sufficient clinical knowledge exists for concluding that probably a like susceptibility to animal foods containing such constituents also exists in men when the function of the thyroid gland is sufficiently disturbed. (14) As regards the thyroid factor in the pathology of exophthalmic goitre, the majority of the symptoms in many patients with that disease can apparently, from an experimental standpoint, be as plausibly explained by the hypothesis of partially deficient thyroid activity as by the hypothesis of augmentation of thyroid function.—*Journal of Experimental Medicine*, 1898, No. 2, p. 147.

The Treatment of Lithæmia.—Dr. Albert C. Barnes believes that the two cardinal rules which sum up the whole subject are: (1) Eliminate the toxic agents which cause the symptoms, and (2) avoid nitrogenous food, from the metabolism of which the toxic agents result. Milk, vegetables, and cereals are the best food; the patient should eat sparingly and of simple food; over-indulgence should be particularly cautioned against, because this is the cause of many cases. To proscribe proteids entirely means to eliminate most of the ordinary articles of food, and is practically impossible. Some nitrogen in the food is required to replace waste. Meat, fish, poultry, eggs, tea, and coffee should occupy an inconspicuous place in the dietary, while carbohydrates, fats, and milk should make part of the list from which the patient may choose. Vegetables in general and fruits are well borne; so also are cereals and small quantities of cheese. Salads of all kinds, fries, sweet articles, and malt liquors are to be avoided. As for eliminants: the treatment is best begun with either a brisk mercurial purge or with small doses of calomel and sodium bicarbonate until free catharsis is produced. If constipation is a marked feature, this must be overcome by carefully adapted doses of cascara with glycerin. The best general eliminants are sodium phosphate and lithium bitartrate. The last is the best diuretic of the lithium salts, and seems to have a specific power upon the alloxuric bodies which are probably the cause of the manifestations. In most cases sodium phosphate has a desirable laxative effect, and its cholagogue action is particularly valuable. This may be given in drachm doses once daily, preferably in a glass of hot water before breakfast, and lithium bitartrate may be taken in five to ten grain doses three times daily in a glass of water. The latter should be given about four hours after a meal. The value of the salicylates in the treatment of lithæmia is decidedly negative. Their powers of elimi-

nation have been greatly over-estimated. It is true that their ingestion is followed by increased excretion of uric acid, but this is due to an increased production of this constituent. It is well known that the salicylates increase leucocytosis; and, as Horbaczewski demonstrated, much of the uric acid excreted comes from the catabolism of the nuclein of the leucocytes. It is, therefore, manifestly improper to administer a remedy which causes increased production of any of the alloxuric bodies. Just at this point the writer would express an opinion, based upon several years of clinical observations, concerning the therapeutic value of the salicylates in those affections for which they are commonly given. In acute rheumatism they are of decided value as analgesics; but in many cases of chronic rheumatism, and in all cases of lithæmia and gout, they are of doubtful therapeutic effect. The excretory activity of the skin is best maintained by frequent bathing. Hot-water baths, taken either every day or on alternate days, are of positive value in the treatment of lithæmia. The reputation of the many lithia waters is probably due more to the water they contain than to any of the salts; at any rate they are not to be relied upon exclusive of other medication. Good pure water, taken frequently during the day in liberal quantities, is to be commended. The general treatment above detailed, viz., the use of a non-nitrogenous diet and frequent bathing, the administration of sodium phosphate and lithium bitartrate, will generally suffice to rid lithæmics of not only the distressing bilious and migrainous paroxysms, but also of the symptoms referable to the gastro-intestinal tract. It is often necessary to treat individual symptoms when pronounced enough to occasion distress. In those cases in which the symptoms of acid dyspepsia are more or less constantly present, which symptoms occasionally culminate in an attack of biliousness or "sick headache," the remedy popularized by Griffith has given excellent results. It is an alkaline aromatic, the formula of which is: Oil of cloves, 2; sodium bicarbonate, 4; chloroform, 1; compound tincture of cardamom, 48; of which a teaspoonful is to be taken after each meal. The writer has found the efficacy of the above mixture increased by the addition of the oil of cajuput in doses of from five to ten minims. In this class of cases, particularly those in which there are present much flatulence and other symptoms of intestinal indigestion, associated with headaches, a compound tablet of bismuth beta-naphtol, containing bismuth beta-naphtol, 3; eucalyptol, ¼; guaiacol, ¼; thymol, ⅓ gr.; given three times daily, is of value. The best results are obtained in the general treatment of lithæmia by adopting a brisk eliminative measure during the first two weeks, then reducing the quantities of the drugs for the second fortnight, then again reducing to a minimum, or intermitting them entirely for the fifth and sixth weeks. In many cases small doses of sodium phosphate and lithium bitartrate given continuously, will keep the symptoms in abeyance. — *Medical Record*, 1898, No. 1429, p. 439.

[The writer apparently does not recognize the fact that the distinction between a meat and a vegetable diet is one of terms rather than of fact. Both are nitrogenous, with the difference that the vegetable albumins are more difficult of oxidation. Further, milk is also albuminous, although it seems to play an important part in diet lists supposedly consisting of carbohydrates and fats in large part.—R. W. W.]

The Effect of Peptones and Albumoses on the Kidney.—Dr. W. H. Thompson gives a preliminary communication dealing with the influence of peptones and albumoses on the kidney when injected into the circulation. The following is a short summary of the results: (1) These substances do not exert so great an influence on the walls of the kidney bloodvessels as they do on those of other splanchnic bloodvessels. (2) They cause a marked increase in the secretion of urine, the maximum occurring during the second hour after injection. (3) The urine secreted is dilute, its percentage of urea and total nitrogen being diminished. (4) The total amount of urea and nitrogen is, notwithstanding, considerably increased. (5) Part of the peptone (or albumose) is excreted during the first hour after injection, but the greater part appears to be retained. The amount so retained, however, is not sufficient to supply enough nitrogen for the increased output of urea and other nitrogenous compounds. He points out that these results were in accordance with what we already know of the diuretic influence exerted by proteid food-stuffs, and also with the period after injection at which their maximum effect is produced.—*Medical Press and Circular*, 1898, No. 3071, p. 277.

Urotropin.—Dr. Leopold Casper finds that this substance does not dissolve uric acid any more than does water. After the entrance of urotropin into the organism some is decomposed into formaldehyde. From experiments it was found that the former was always detected in the urine and sometimes in the blood; the latter sometimes in the blood and generally in the urine. The reason of this is probably that there is a combination of formaldehyde with albuminous substances in blood or urine so that its presence cannot be determined. As to the elimination of urotropin and formaldehyde, both are found after ten minutes have elapsed since its administration. Fourteen days after the last dose the urine of a patient showed both substances; generally the period of elimination is shorter. Clinical reports are appended showing the value of this remedy in phosphaturia, severe ammoniacal cystitis, and long-standing severe pyuria.—*Monatsberichte der Krankheiten des Harn- und Sexual-Apparates*, 1898, No. 1, S. 1.

Dosage in Anæsthetics.—Dr. A. Waller looking closely into the reports of deaths, it appeared that these had occurred because chloroform had been improperly administered, from ignorance or carelessness, probably the former. Snow, forty years ago, made a statement that to produce the second stage of anæsthesia, 12 minims of the anæsthetic [chloroform] in the blood are necessary; to produce narcotism of the third degree, about 18 minims are necessary; while to produce full surgical anæsthesia, 24 minims are required. To produce death requires double the minimum amount which produces the minimum amount of anæsthesia, namely, 36 minims. From the results of physiological work it came out with remarkable coincidence that the lethal dose of chloroform was twice the anæsthetic dose. If a rough calculation of the average fluids of the body is taken, the amount of chloroform present in the blood which is necessary to anæsthetize a mammalian animal, including man, is between 1 and 2 per cent.; the maximum should not be exceeded. Toward procuring safety in administration, the first step is to recognize the fact that, as regards the rough and ready use of an anæsthetic, one may not

take chloroform and ether as being at all on the same footing. In using the former we deal with a weapon seven times as powerful as is ether. This is especially important in minor surgery, for it is here that nine-tenths of deaths from anæsthetics occur. As to the safe use of chloroform, it was a question of measurement—a question of quantity per time—that must be aimed at in order to abolish death by chloroform. There should be some agreement as to quantity among anæsthetists. Uniformity of strength cannot be obtained in an "open method" of inhalation. Some method must be adopted which shall enable the anæsthetist to know how much chloroform is being given per minute.—*The Clinical Journal*, 1898, No. 284, p. 426.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

PROFESSOR OF MEDICINE IN THE JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

GEORGE DOCK, M.D.,

PROFESSOR OF MEDICINE IN THE UNIVERSITY OF MICHIGAN.

Persistent Ductus Arteriosus Demonstrated by X-rays.—ZINN (*Deutsche med. Wochenschrift*, 1898, No. 11, Vereins-Beilage) reports a case: A woman of thirty-seven years had always been delicate as a child, menstruated first at twenty-six; had a rickety pelvis, but was able to work as a domestic and complained only of dyspnœa on exertion. Physical examination showed pallor, no cyanosis, the terminal phalanges clubbed, nails poorly developed. The heart-dulness extended from the right edge of the sternum to within a finger-breadth of the left nipple line. From the first to the third left intercostal spaces there was an area of dulness five to six centimetres wide. There was a thrill over the area of heart-dulness, strongest in the first left interspace, and a very loud systolic murmur, with weak first and accentuated second sound. In the great vessels the loud murmur was also audible. On examination with the fluorescent screen the position of the heart was readily made out, corresponding to the area of dulness, and also a dark area corresponding to the one in the second and third interspaces. This was no doubt the dilated pulmonary artery, the occurrence of which in case of persistent arterial duct was shown by Gerhardt.

Tic Convulsif in a Case of Hemiplegia.—HABEL (*Deutsche med. Wochenschrift*, 1898, No. 12) has observed this very rare occurrence. Tic began in 1895, in the left side, about the same time with severe and repeated epistaxis, but continued after the bleeding stopped. In August, 1897, apoplexy came on without prodromes. Loss of consciousness lasted an hour, and was followed by aphasia and complete left-sided paralysis. In a few days speech

returned and motion was possible in the left leg, but the arm was still paralyzed. On admission there was hemiplegia with contracture of the left arm. The inferior facial nerve was paralyzed, but the left side of the face was the seat of an exquisite tic convulsif. Several times a minute the angle of the mouth and the alæ nasi were drawn up by clonic contraction of the affected muscles. The spasm continued during sleep, and was not influenced by eating. Excitement rendered it more frequent. Sensibility of the face was preserved. The other conditions were as in any case of hemiplegia. The case illustrates an experiment of Cadiot, Gilbert, and Roger, who removed successively the cortical centre and hemisphere in a dog that for seven years had tic convulsif, without affecting the spasms, which only ceased after the facial nucleus in the pons was destroyed. In Habel's case the author thinks the symptom was due either to a direct irritation of the facial nerve at the base of the brain or to a reflex. The latter supposition is based on the history of nose-bleed in the beginning, a redness of the mucous membrane in the posterior nares, and the relation of tic in certain cases of nasal polyp to the latter.

Thyroidism and Basedow's Disease.—NOTTHAFFT (*Centralblatt f. inn. Med.*, 1898, No. 15) makes a suggestive contribution to this interesting subject. A man of forty-three, always healthy, not neurotic, of good habits, began to take treatment for increasing obesity. Failing to get satisfactory results by various reduction methods, he began, without medical advice, to take thyroid tablets. These, of five grains each, he took in doses of from nine to forty-five a day, and in about five weeks had taken almost a thousand. The loss of weight during this time was thirty pounds (from two hundred and twenty). By the end of the third week, while taking thirty tablets a day, the patient began to cough, and about the same time the neck began to swell. By the end of the fourth week there were palpitation and loss of sleep, later thirst. He reduced the number of tablets, and in the beginning of the sixth week consulted the author. The circumference of the neck had increased three centimetres, the patient was excitable, depressed, could not sleep, the latter depending partly on the exaggerated beating of the carotids. It appeared that the loss of weight came on suddenly, about the time the subjective symptoms began. On examination it was found there was exophthalmos, thick neck without visible enlargement of the thyroid, but the latter could easily be felt to be enlarged. There was moderate tremor, the skin was cool and moist. The pulse was soft and regular, 120 in the minute; the carotid and brachial arteries pulsated visibly. The apex beat was in the fifth interspace inside the nipple line, strong and diffuse. Graefe's and Stellwag's signs were present, but the pupils, reaction, vision, and adduction were normal. The urine, amounting to three litres a day, contained 1 per cent. of glucose. The thyroid medication was stopped, a hypnotic and Fowler's solution ordered. In ten days the psychic symptoms improved, the others later, and in four weeks the tremor, glycosuria, and tachycardia had stopped, but the struma, exophthalmos, and other ocular symptoms persisted half a year, and then gradually subsided. After gaining ten pounds the patient began to take five-grain doses of iodo-thyrin three times a day, without bad effects. It is important to note that in this case some of the characteristic symptoms of

so-called thyroidism were absent, viz., headache and rheumatic pains. For these reasons the author seems justified in looking on the case as one of Basedow's disease due to excessive thyroid consumption. A symptomatic Basedow's disease on the basis of a thyroiditis seems negatived by the absence of fever and local signs. The article ends with a theoretical discussion of the nature of Basedow's disease, in which nothing new is brought out, but which covers the previous literature quite thoroughly.

Beri-beri in Sucklings.—HIROTA (*Centralblatt f. inn. Med.*, 1898, No. 16) has made an important observation on a disease in infants nursed by mothers with beri-beri. It has been thought that beri-beri never occurred in children before the second dentition. The author, however, has been able to see fifty-two cases of the affection in infants of from one to thirteen months. All were nursed by women with beri-beri. Five died, five more could not be followed up. Medicines had no effect on the symptoms, but all the cases that recovered did so within a few days after the patients were put on cow's milk, condensed milk, or nursed by healthy women. From the rapidity of the improvement it could hardly be thought that the symptoms were due to anything but an intoxication from the milk. A comparison of the symptoms shows a close resemblance with those of beri-beri in the adult. Diarrhœa, uncommon in adults with beri-beri, was sometimes present, and the indican reaction almost always present in beri-beri was absent (perhaps on account of the diarrhœa). The author looks on these observations as proving that beri-beri is the result of an intoxication, although he has been unable to find the toxic substance.

Valsalva's Experiment in Open Pneumothorax after Costal Resection as a Measure of the Expansibility of the Lungs.—REINEBOTH has made some interesting experiments on this subject, taking sphygmograms while the patient made expiratory efforts with the mouth and nose [or the glottis] closed. A number of clinical histories are cited, with tracings, which indicate that the method may have considerable prognostic value. In order to obtain trustworthy results it is essential that the resection opening permits the passage of air, and cannot be closed by the lung or diaphragm. In case of pneumothorax of large size the sphygmogram taken during Valsalva's experiment will not show the usual rise of venous congestion if there is a large fistulous opening between the bronchial tree and the pleura, or if the affected lung is capable of expansion. If we can exclude the first possibility the method indicates whether the lung is impossible or difficult to expand. From the author's results the method seems more reliable than the manometric one, or that by filling the cavity with water.—*Deutsches Archiv f. klin. Med.*, Bd. 60, p. 111.

The Blood Changes in Typhoid Fever.—KÖLNER (*Deutsches Archiv f. klin. Med.*, Bd. 60, p. 221) has made extensive examinations which confirm a number of previous observations and clear up certain contradictions. The author is at times too optimistic. He thinks the leucocyte count is of value in distinguishing typhoid fever from general miliary tuberculosis, but both Cabot and Warthin have shown that the latter disease, like typhoid fever,

may show a subnormal number of leucocytes. In uncomplicated typhoid fever Kölner never observed leucocytosis. Usually the number was subnormal, even as low as 1000 per c.mm. There was no positive relation between the number of the leucocytes and the temperature. In some cases the count fell as the disease became worse. The author thinks that in general the number of leucocytes is less in the second and third than in the first and fourth weeks, and that in convalescence the leucocytes increase, sometimes above normal. Age does not seem to affect the results. [The author did not examine any cases in children.] The condition of the leucocytes in the complications of typhoid are interesting. In many cases with suppurating complications [streptococcus pneumonia and otitis media, decubital abscess, bronchitis], in intestinal hemorrhages [two out of three cases] there was no increase of leucocytes above normal. In one case of hemorrhage there was temporary leucocytosis [to 9300], and in a case with severe course and obscure abdominal symptoms there was increase to 11,200 leucocytes. The author properly warns against placing too much reliance on the blood examinations alone, but thinks the hypoleucocytosis more reliable than roseolæ, enlarged spleen, typhoid stools, or the fever course. Prognostic value the matter has none. Kölner found the red corpuscles constantly diminished in typhoid fever, the hæmoglobin also, and to a greater degree. These began very early, though sometimes masked by various conditions that cause a concentration of the blood. The hæmoglobin usually reached its lowest point before the end of the defervescence, but sometimes remained at this point or even continued to fall. In some of the latter cases there were explanations for the further fall in the faulty nutrition of the patients. In convalescence the improvement was rapid, usually in proportion to the previous fall, and the corpuscles often showed greater variations than the hæmoglobin.

Intestinal Auto-intoxication at the Congress for Internal Medicine.—The discussion showed slight tendency to unanimity, both as to pathology and therapeutics. MÜLLER held that intoxications from the intestinal tract are not auto-intoxications properly speaking, because they are due to saprophytic germs in the stomach and intestines. Many so-called auto-intoxications are really instances of unrecognized food-poisoning, not necessarily due always to toxins or toxalbumins. It is very doubtful whether albumin-putrefaction in the intestine causes symptoms of poisoning; the products of intestinal germs are very slightly toxic. But the occurrence of autochthonous decomposition of the intestinal contents cannot be doubted. The severity of the symptoms in many cases of gastro-intestinal disease, especially in children, points to the possibility, as do also certain skin diseases (*e. g.*, urticaria) occurring in the course of intestinal disturbances. So-called idiosyncrasy is often vasomotor anomaly from an intestinal reflex. Müller condemned the French doctrine of auto-infection as exaggerated, resting as it does partly on erroneous ideas about the normal bacteria of the mouth, pharynx, etc., and claimed that what is called auto-intoxication is really infection acquired often by contagion. Müller decried all medicinal so-called intestinal antiseptics. Calomel is cathartic rather than antiseptic. Lavage and cathartics are useful. BRIEGER spoke of the lack of exact chemical knowledge on the subject, and especially that regarding the toxicity of the urine. The potash

salts of the urine are innocuous to human beings; Bouchard's urotoxic coefficient is a very doubtful factor. The toxicity of the urine can only be considered established when the poisonous substance has been isolated, and in any event is not very great. As to intestinal antiseptics, BRIEGER agreed with Müller, though suggesting the possibility of serum antitoxin treatment. ALBU held to the theory of auto-intoxication in many cases rather than the antiquated and inadequate reflex theory, though admitting the impossibility of chemical proof at present. Not only Bouchard's urine method, but also Albu's own method, by testing the toxicity of blood-serum, is ureliable, though from experiences with these we may infer that in many cases spontaneous changes in the physico-chemical conditions in the body set up abnormal metabolic changes. QUINCKE recommended yeast in pure culture, up to 150 c.cm. internally, as a remedy for intestinal decomposition. ROSENHEIM also had used yeast with success, but recommended menthol also. STERN and FÜRBRINGER claimed a certain value for calomel. BOAS said that in intestinal auto-intoxication there was often a renal insufficiency. Calomel acted at the same time on the bowels and kidneys. For excessive formation of intestinal gas salicylic acid was useful. STRAUSS had found both menthol and thymol useful in preventing the putrefaction of stools.—*München. med. Wochenschrift*, 1898, No. 17.

The Urine in Pneumonia.—F. PICK, at the recent Congress for Internal Medicine, called attention to a change in the urine in pneumonia not hitherto noticed. In twenty-four to forty-eight hours after the crisis the urine shows a marked fall in acidity, becoming neutral or even alkaline. This phenomenon, observed in thirty-one out of thirty-eight cases, remains for a day or a day and a half, and then the acidity returns. Pick explains the change as perhaps due to the absorption of the exudate, especially of the large quantities of sodium in it.—*München. med. Wochenschrift*, 1898, No. 17.

The Water and Alkali of the Blood in Nephritis and Uræmia.—BRUNER (*Centralblatt f. inn. Med.*, 1898, No. 18) reports some observations that if confirmed and extended will add much to our knowledge of some obscure conditions. One of the most constant alterations in the blood in nephritis, according to him, is an increase of water in the serum. This has no constant relation with œdema. The blood-serum may be more dilute in cases with excessive diuresis and slight œdema than with the latter conditions reversed. It is difficult to discover whether albuminuria has any influence on the dilution of the serum, and if so, how much. Most evident and certain is the effect of uræmia on the blood as a whole. Distinct symptoms of uræmia were always associated with dilute blood, without regard to œdema, albuminuria, and amount of urine. In one case the difference in the amount of water in the uræmic and free stages was 3 per cent. In another case, in the free period, with marked œdema, there were 17.22 per cent. of solids; in the uræmic stage, with slight œdema and 1500 c.cm. of urine, 14.80 per cent. The dilution of the blood in uræmia seems to depend on an increase of the serum. In one case of uræmia there was no dilution, but on the other hand, the author observed no instance of greatly diluted blood without uræmia, although in chronic nephritis with cachexia this, of course, occurs. In the cases in

question the uræmic symptoms were well marked. The author thinks that examinations of the blood may clear up the classification of the various states included under the term uræmia. He also thinks that œdemas and dropsies are modes of preventing an excessive dilution of the serum, and remarks on the fact that nephritic patients often feel comparatively well as long as the dropsies persist. Another characteristic of the blood in nephritis is the decrease in sodium, which also probably has an important rôle in the pathology of the disease. Practically, the author thinks the variations in the water of the blood may be of value in the prognosis. The determination may be made by Stintzing's method, with a few drops of blood, though it is better to use larger quantities, taken with a wet cup or a syringe. The use of cathartics to produce watery stools in uræmia receives a rational explanation from these observations, and the systematic use of large amounts of sodium salts seems worth trying.

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

PROFESSOR OF CLINICAL SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE UNIVERSITY AND PHILADELPHIA HOSPITALS;

ASSISTED BY

ALFRED C. WOOD, M.D., INSTRUCTOR IN CLINICAL SURGERY, UNIVERSITY OF PENNSYLVANIA; ASSISTANT SURGEON, UNIVERSITY HOSPITAL.

AND

C. L. LEONARD, M.D., ASSISTANT INSTRUCTOR IN CLINICAL SURGERY IN THE UNIVERSITY OF PENNSYLVANIA.

A Fatal Case of Forcible Reduction in Pott's Disease—VULPIUS (*Cent. f. Chir.*, December 11, 1897), speaking of forcible reduction in Pott's disease, recommends that spinous processes be connected together by small bone periosteum flaps, so that later they may become united by a bony band of union. In applying the plaster-of-Paris jacket he advises that the patient be suspended after the correction in the ordinary manner employed when applying these jackets—that is, in a vertical position, after the correction has been effected. The application of the jacket is greatly facilitated by this manœuvre, and it seemingly has a beneficial effect upon the action of the anæsthetic.

The author reports the death of a five-and-a-half-year-old boy during this operation while the jacket was being applied in the manner usual in these cases. After the forcible extension and during the application of the jacket, clonic cramps in the limbs, gnashing of the teeth, and contracted pupils ushered in a collapse that was fatal, and from which the patient was not resuscitated by removing the jacket and restoring the curvature. A partial post-mortem only was allowed, and disclosed no sufficient cause in any injury of the cord or its membranes.

Idiopathic Dilatation of the Colon.—In reference to the cases reported under this title, TREVES (*The Lancet*, January 28, 1898) says that it is safe to say that in certain portions of the alimentary canal extensive dilatation may occur which is independent of any obstruction of the lumen of the tube. To such forms the somewhat vague term "idiopathic" may, with a scarcely less vague reason, be ascribed.

The cases reported may be divided into two classes. In one series of cases the patients are adults, are mostly males, and are over fifty years of age. In the second series of cases the patients are children, and symptoms of abdominal trouble have been more or less apparent from birth.

Of the first class, he says that the majority of the examples of so-called "idiopathic dilatation of the colon" occurring in elderly subjects appear to be examples of simple dilatation of the bowel above an imperfect but definite obstruction. With regard to the cases of "idiopathic dilatation of the colon" in children, it appears to the author that they have less claim to the title "idiopathic" than the other class of cases.

The evidence obtained from the perusal of these cases very strongly suggests that the great majority of them, at least, depend upon a congenital narrowing of the lower extremity of the large intestine. The case reported by the author exhibited in a marked degree the features of "idiopathic dilatation of the colon," as shown by an enormous distention of the abdomen, the obstinate constipation, the hypertrophy of the lower part of the colon, and the practical failure of all purgative measures. The case indeed may be taken as a quite typical example of trouble described under this questionable title. Operation, removing the whole of the bowel below the transverse colon, relieved the symptoms, the child making an easy recovery. The examination of the bowel, however, made it evident that the distention was not "idiopathic," but was due to congenital narrowing, regular and uniform in degree, of the lower end of the colon. Indeed, the rectum and sigmoid flexure were found to be defective in length and to be represented by a narrow and contracted tube of uniform calibre.

The author cites a number of cases from literature, and says of them: All of these cases have certain very striking features in common. Distention of the colon and obstinate constipation have been noticed practically from birth; the distention has been extreme, and has mainly involved the lower sections of the colon; the wall of the bowel has been greatly hypertrophied. Movements of the hypertrophied coil have been visible through the parietes; relief of the bowel has been effected almost solely by enemata. Certain secondary conditions, such as catarrh and ulceration of the distended gut, with possible tearing of its walls in extreme cases, have been noted. All the cases except one, perhaps, in which an artificial anus was established, appear to have ended fatally. The general circumstances of these cases do not seem to be consistent with the idea of an "idiopathic dilatation of the colon." The very prominent feature in every example of the trouble has been some obstruction in the lower part of the large intestine. The conditions presented are not comparable with those met with in idiopathic dilatation of other parts of the alimentary canal to which attention has been directed.

The author ventures to think that all cases of "idiopathic dilatation of

the colon" in young children are due to congenital defects in the terminal part of the bowel, that there is in these cases an actual mechanical obstruction, and that the dilatation of the bowel is not idiopathic. The marked hypertrophy of the distended gut suggests in the most emphatic way that there is an obstruction to be overcome, and such hypertrophy is quite inconsistent with the conception of "idiopathic" dilatation of the bowel.

The author reports a case in which he first established an artificial anus with considerable relief of the symptoms which were typical of the so-called idiopathic dilatations. There was, however, a distinct, even, and extensive congenital narrowing of the lower extremity of the colon. He finally had recourse to a complete excision of the bowel, including the descending colon, the sigmoid flexure, the rectum, and anus. The transverse colon was brought down and sutured where the rectum had been removed. The child made a perfect recovery and is markedly benefited.

A Case of Complete Removal of a Multilocular Cyst of the Pancreas; Recovery.—An interesting case in which the diagnosis was not made prior to operation by a number of distinguished consultants is reported by MALCOM (*The Lancet*, January 29, 1898). The patient was a married woman, forty-five years of age, who had noticed a swelling in the abdomen about seven months earlier, her attention having been drawn to the part by a slight tenderness. The swelling had grown rapidly since. The growth was readily felt in the left loin by bimanual palpation. It appeared to be from five to six inches in length, and more or less uniformly rounded. Its greatest bulk was below the costal margin, but it was freely movable, and could be pushed with particular ease upward and backward until about three-fourths of it were overlapped by ribs. The percussion note over the upper part of the anterior and outer aspects of the growth was dull; over the lower and inner parts the note was resonant. The percussion note was slightly duller over the ordinary position of the spleen than over the neighboring lung tissues, this impaired resonance being quite separate from the abnormal dulness over the tumor in the abdomen. The right kidney was palpable and appeared to be of normal size and somewhat movable. The tumor had no connection with the pelvis. The examination of the urine had never shown any abnormality. The growth was believed to be renal, at first malignant; but as it did not increase in size, and the patient gained in weight up to the time of consultation, it was concluded that it was a case of hydronephrosis. Three consultants concurred in this diagnosis. It was decided to remove the kidney. The operation showed that the right kidney was normal in shape, size, and consistence, quite smooth on its surface, and slightly more mobile than usual. The tumor was larger than had been supposed, and more irregular in outline. The transverse colon lay in front of it. Above the colon the tumor was covered by peritoneum and connective tissue. The kidney was found immediately behind the cyst, and the lesser sac of the peritoneum was not opened. A very thin-walled and obviously multilocular cyst was exposed, some of the loculi being of a deep venous color, and others almost white. The tumor had more the appearance of one of those rare congenital cystic degenerations of the kidney than anything the author had seen in this part of the abdomen. Its true nature was not discovered until it was all but com-

pletely enucleated, when its attachment to the tail of the pancreas showed its true nature. Very free hemorrhage occurred after the stump, which had been transfixed and ligated, was returned into the depths of the wound. Traction on the stump stopped the bleeding, and it was with great difficulty that the bleeding point was detected.

Twenty-two Consecutive Arthrotomies of the Knee.—O'Conor (*The Medical Press*, January 26, 1898) reports a series of cases of arthrotomy for both acute and chronic conditions of the knee-joint, which he has treated within the past two years without any particular selective process in the choice of the cases.

"The rheumatic patients were operated on because the function of their joints seemed doomed, and in one case the treatment was undertaken as a forlorn hope to save the patient's life.

"No apology is necessary for the drainage of gonorrhœal knee-joints, as all expectant plans have proved utterly futile; neither does the removal of blood and clots need any qualifying remark further than that it is a surgical obligation. As to traumatic 'water on the knee,' in my opinion, no method of treatment has a brighter future before it than arthrotomy and drainage.

"All the joints were irrigated during operation with mercuric lotion, and in five cases it was repeated daily. Drainage was continued in each instance until the serous discharge had ceased, and nothing but normal synovial fluid was seen trickling from the wound. Splints were only used in six cases, and were early discarded. Active movement was enforced as soon as the gauze drain was dispensed with, and in not a single case was there cause for post-operative anxiety."

All of the cases reported recovered with perfect function, and the author believes that these cases tend to prove the efficiency of surgical treatment in some of the common affections of the knee-joint.

The Relation of Tubercular Disease of the Shoulder-joint and Caries of the Coracoid Process.—Wolff (*Cent. f. Chirg.*, 1898, No. 6) says that in nine cases of tubercular disease of the shoulder-joint operated upon by Bardenheur in the past year, three had in addition carious disease of the base of the coracoid process, and that it is this portion of the coracoid that is most frequently affected.

The appearance of the disease in this locality is secondary to the tubercular involvement of the joint itself. The tubercular infection passes from the diseased joint through the glenoid cavity into the neck of the scapula, and thus reaches the base of the coracoid process. If the cavity of the glenoid is infected and the coracoid process, there is undoubted evidence that the neck of the scapula is also involved, and it must, therefore, be included in any radical operation directed toward the removal of the disease.

Surgery of the Kidney.—In his Hunterian Lecture upon this subject, Morris (*British Medical Journal*, March 26, April 9 and 16, 1898) emphasizes the facts (1) that the errors and uncertainties in the diagnosis of renal calculus have in many instances been of distinct advantage, because they have led to the exploration of the kidney, and thus in turn to the discovery and

cure of various morbid conditions other than those due to stone. (2) That unsuspected, quiescent, and migratory renal calculi cause very destructive and even fatal consequences, and that we ought to revise our practice with regard to the early treatment of stone in the kidney. (3) That the low mortality of nephrolithotomy and the high mortality of nephrotomy (that is, the operation performed for advanced disorders due to renal calculus) show the advisability of operating at as early stage as possible.

The author places these affections in the very forefront of surgery of the kidney, for the following reasons:

1. They are the most painful and frequent of the surgical diseases of the kidney. Probably no disease, except acute tetanus, is capable of causing worse suffering.

2. Renal calculus, while slowly destroying the kidney, often physically disables its victim by its unrelenting irritation and its unyielding resistance to every form of medical and dietetic treatment.

3. No disease gives rise to such a variety of morbid changes in the kidney as calculus; and none is more certainly fatal when allowed to progress without surgical interference.

4. Few operations in surgery are so successful as nephrolithotomy, by which a calculus is removed from a kidney not disorganized by the calculus or otherwise. No great operation is followed by a smaller mortality. Nephrolithotomy gives absolute cure, saving the kidney from progressive destruction and the patient from what may prove at any time imminent danger to life.

5. Renal surgery will grow in confidence and favor with the profession and the public as nephrolithotomy anticipates and displaces nephrotomy and nephrectomy.

The conclusions arrived at by the author from his study of the surgical treatment of these affections are:

1. That the aim of surgical treatment of renal calculus should be to extend the application of nephrolithotomy, and thereby restrict the necessity of nephrotomy and nephrectomy.

2. That more frequent than not the failure to find a stone is not in reality a failure of treatment, because there are so many curable morbid conditions which mimic renal calculus and which are discoverable only by exploration.

3. That the theory that a stone in one kidney, whether that kidney is painful or not, reflects or transmits pain to the opposite kidney is quite unproved; that it is a dangerous theory, calculated to lead to very erroneous practice, and that the surgical principle with regard to exploratory operations should be that with pain, paroxysmal or continuous, on one side only, the kidney on the painful side should be explored.

4. That nephrectomy for calculous conditions is not often called for, and should be done only in exceptional cases. Nephrotomy for calculous pyonephrosis is the proper operation, at any rate as a primary operation, because of the frequency of double calculous disease. Experience has shown that kidneys from which stones weighing 830 grains and 1300 grains have been removed are functionally sufficient to maintain life during the blocking of the ureter or suspended action of the kidney of the opposite side.

5. That nephrectomy whilst the opposite organ is occupied by calculus is

fraught with the greatest danger to life; whereas nephrectomy after the opposite kidney has been freed from stone, will probably be followed by recovery from the operation, and possibly by very good health for many years afterward.

6. That when renal calculus causes reflected or transferred vesical or ovarian pain, the removal of the calculus will be followed by complete cure of the bladder or ovarian symptoms.

7. That in some cases renal calculous conditions are attended by very remarkable nervous symptoms, sometimes with, sometimes without, high temperature, and that information as to the cause of the symptoms is needed.

8. That unsuspected renal calculi are a source of very real danger to their possessors; and when, whether by accident or by systematic examination of the urine, we have cause to suspect the presence of a calculus, we should recommend its immediate removal, regardless of the fact that it is not causing renal or transferred pain.

9. That quiescent calculus is as dangerous to the individual as unsuspected calculus, and ought to be removed by operation.

10. That the hitherto accepted teaching that a renal calculus, if causing only mild symptoms, or attacks of colic of only recent occurrence, should be treated on the expectant plan, ought to be discarded as unsound in theory and dangerous in practice.

11. That the same principle should be applied to renal calculus which has long been the rule in regard to vesical calculus, namely, when suspected it should be searched for, when known to exist, removed, without waiting in the hope that it may become encysted or spontaneously expelled.

12. That the very low mortality of nephrolithotomy puts this operation upon the same footing for renal calculus as lithotomy in the most experienced hands for vesical calculus.

In regard to fistulæ occurring after the operation upon a kidney the seat of pyonephrosis or a fistula which has formed by the spontaneous opening of such an abscess, the author says: The closure by surgical treatment is tedious and sometimes impossible; and in some cases, after having been successfully treated and remaining closed for many months or a year or two, it will reopen.

Those which do not communicate with the kidney or ureter should be treated on the ordinary principles applicable to all fistulæ; those which do so communicate must be dealt with differently in different cases. If there is a calculus in the kidney it must be removed; if the kidney is quite disorganized, nephrectomy is requisite; the fistulous tract should be cut out and the cut surfaces united by sutures. When no stone is found in the kidney the ureter will probably be the seat of some kind of obstruction.

The two objections generally raised to early operation for renal calculus are: (1) That the calculi will be missed if sought for very early, because of their small size; (2) that very small calculi, if they once enter the ureter, pass through the urinary passages without risk to life. The author holds that both of these are unsound and lead to dangerous delay.

The author's cases show that very minute calculi are readily found. They are capable of producing the complete destruction of the kidney, or may become the immediate cause of death from suppression of urine.

One of the gravest dangers from minute calculi is the production of calcu-

lous anuria, which is one of the most fatal complications of renal lithiasis. The operations for this form of renal disease are, even now, not performed sufficiently early or often, and the symptoms of the disease seem to be imperfectly known or not fully appreciated.

Calculous anuria occurs when the ureter or renal pelvis of the kidney is occluded by a calculus, the other kidney being absent, or atrophied, or diseased. It often affects persons in robust health, and may be sudden and complete in its onset. It is then due to the cessation of function of a kidney which has undergone compensatory hypertrophy, and which up to the moment of obstruction has been secreting the whole or chief part of the urine. Occlusion of one ureter never gives rise to fatal anuria if the opposite kidney and ureter are normal.

The occurrence of former attacks of renal colic in a gouty person, followed by the sudden onset of pain on one side, and this accompanied or immediately followed by anuria, point at once to obstruction of a calculous nature. The diagnosis will be further strengthened if a swelling or distinct tenderness on pressure is present in the renal region or in the course of the ureter of the side recently become the seat of pain. If there is no clear previous history the diagnosis is more difficult.

In making a diagnosis the course of the ureter should be palpated where possible through the abdominal parietes; the ureter frequently remains inflamed and painful after the passage of a calculus. Rectal and vaginal examinations may yield more serviceable results. Catheterization of the ureters is of little value in assisting the diagnosis in these cases.

In the treatment nephrotomy should be performed in the gravest cases, to prevent death from uræmia; in the slighter and intermittent cases, to extract the stone which at any time may produce complete persistent anuria.

An operation ought to be performed as soon as the anuria is established and the diagnosis is satisfactorily made. The operation is serious because of the urinary suppression produced by the obstruction, the poisoned condition of the blood produced by the suppression, and the structural changes in the kidney.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

PROFESSOR OF DISEASES OF THE EYE IN THE PHILADELPHIA POLYCLINIC; SURGEON TO WILLS EYE HOSPITAL, ETC.,

AND

T. B. SCHNEIDEMAN, A.M., M.D.,

PROFESSOR OF DISEASES OF THE EYE IN THE PHILADELPHIA POLYCLINIC; ASSISTANT SURGEON TO WILLS EYE HOSPITAL, ETC.

Ocular Palsies Through Metastatic Carcinoma.—ELSCHNIG (Vienna) reports two cases, the palsy being in one due to metastatic tumors in the muscles, and in the other to metastatic involvement of the cavernous sinus.

The first was a case of uterine carcinoma, with involvement of lymphatics, skin, and right breast. In the left orbit all the muscles except the inferior oblique presented metastatic tumors close to their origin, which on microscopic examination proved to be carcinomatous. The nerve fibres passing through them were found atrophied. There had been protrusion of the eyeball, almost complete immobility, and anæsthesia of the cornea with neuroparalytic keratitis. The pupil, however, had remained unaffected.

The second patient had paralysis of all the ocular muscles, with normal acuteness of vision and normal fundus, and no exophthalmos. He suffered from carcinoma of the thyroid, which perforated the right jugular vein, causing thrombosis of the right pulmonary vein and metastasis in the left cavernous sinus.

Cases of metastatic tumor in the muscles have been reported by Horner, where the paralysis was due to neoplasm at the base of the skull; and by Meigs and de Schweinitz, where metastatic carcinoma of the brain extended along the nerves into the orbit. But paralysis of the ocular muscles due to this cause is excessively rare.—*Wiener klin. Wochenschrift*, 1898, No. 5.

Coloboma of the Iris.—ANGUS MCGILLIVRAY (Dundee) reports a case of upward coloboma of the iris, with subluxation of the lens downward in the right eye, the left having been lost by inflammation in earlier life. The dislocated lens was opaque, and its extraction restored full vision.

Cases of upward coloboma are extremely rare; the usual position being that of the fœtal cleft downward or a little inward. Cases like this can be scarcely explained by deficient closure of the cleft, such complete transposition of it, not occurring. Nor is incomplete coloboma thus explained, or by delayed separation of the crystalline lens from the cornea. Impaired development of a part of the ciliary ridge is thought to explain the coloboma and defect in the zonule in this case, as well as in such anomalous forms as "keyhole" and "bridge" coloboma.—*Ophthalmic Review*, January, 1898.

Operative Treatment of Glaucoma.—DR. STÖLTING (Hanover), experimenting on the eyes of rabbits, produced great increase of tension by ligation of the vorticose veins. This increase of tension commenced at the completion of the ligation, increased until within a few hours the eyeball was excessively hard. The iris was pushed forward usually in contact with the cornea; the pupil partly dilated and immobile, and the aqueous became discolored with blood, and later considerable hemorrhage occurred in the eye. Microscopic examination of the eyes so treated showed marked thickening, infiltration, and softening of the limbus. In one case, at the end of twelve hours the eye was found ruptured just outside of the limbus, the lens having escaped and the globe being filled with coagula.

Stölting believes that this eye was ruptured by a blow, but has noted that rupture is apt to occur in this situation with abscess of the globe caused by infection. The central portion of the cornea and other parts of the sclera showed but little or no infiltration. He believes that it is the relief of this zone of infiltration at the limbus which gives value to such operations as iridectomy and anterior sclerotomy. Even Hancock's operation, called division of the ciliary body, opens this infiltration-ring, and so may be bene-

ficial. Posterior sclerotomy, on the other hand, can only relieve the space between the choroid and the sclera, leaving the anterior filtration channels unopened.—*Transactions Heidelberg Ophthal. Congress*, 1897.

[The especial liability of the limbus to infiltration, if confirmed by other observations, together with the fact that the whole of this infiltration circle can communicate with and so drain through an opening made into one part of it, through the spaces known as the canal of Schlemm, offers the best explanation yet suggested of the curative power of iridectomy and other allied operations.

The fact that after organization of an exudate drainage would have little influence in removing it will also serve to explain the comparative inefficiency of operative treatment in chronic glaucoma.—J.]

The Mechanism of Eye-movements.—C. WEILAND (Philadelphia) urges that the common assumption of any complete antagonism of one ocular muscle to another, the internus to the externus, the superior to the inferior rectus, and the superior to the inferior oblique, is not correct; that the muscles do not act in pairs, each of a pair tending to rotate the eyeball in opposite directions about the same axis; but that each individual muscle tends to rotate the eyeball about an axis peculiar to itself, and therefore no one muscle can perfectly antagonize another, and no two muscles acting harmoniously can alone direct the two eyes toward a particular point. In all or almost all eye-movements, all of the muscles participate in varying degree. The weakness of one muscle can often be compensated by increased action of others.

Weiland makes some very interesting and instructive calculations regarding the shares which the different muscles take in the causation of certain movements of the eyes, and he urges that the assumed simplicity of the ocular movements is incorrect and misleading. His calculations are based on the determinations of the muscular attachments made by Volkmann.—*Archives of Ophthal.*, 1898, No. 1.

[Weiland's paper, although quite technical, is an important one. The simple working out of the numerical values of the traction exerted by each of the several muscles in causing a certain movement of the eye emphasizes, as nothing else can, the extremely complex nature of the common ocular movements. To some extent it is a *reductio ad absurdum* of the anatomical method of studying eye-movements and their disorders. Anatomical conceptions regarding these movements have value, but it becomes very evident that they must be supplemented by a better understanding of such movements from the side of their physiological relations.—J.]

Operation for Ptosis.—W. H. WILDER (Chicago), for complete paralytic ptosis, employs the following operation: An incision one inch and a half or more in length is placed where the scar will be concealed by the eyebrow. The lower lip of this incision is drawn down and the skin and muscle carefully dissected from the fascia down to the tarsus. Two sutures of fine sterilized catgut or silk, armed at each end with a curved needle, are then passed in the following manner:

The first needle is introduced deep enough into the tarsus to secure a firm

hold at a point about at the junction of the outer and middle third and a little distance from its convex edge. It is then drawn through, and with it several gathering stitches are taken in the tarso-orbital fascia, after which the needle is made to pass through the muscle and connective tissue of the upper lip of the wound. The other needle on the same suture follows a parallel course in the same manner, entering the tarsus about three millimetres from the point of entrance of the first, then gathering the fascia into small folds and emerging in the tissue above, thus making a loop by which the lid may be drawn up.

The second suture is passed in the same way, making a loop at the junction of the middle and inner third of the tarsus. The requisite elevation of the lid may be now secured by drawing on the loops and tying the sutures, which are to be buried in the wound.

The lower lip of the wound is now united to the upper with fine sutures. The slight scar that remains after healing is almost entirely hidden when the eyebrows grow again. The buried sutures become encapsulated and give additional strength to the folds of fascia that hold up the lid.—*Annals of Ophthal.*, 1898, No. 1.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,

OF PHILADELPHIA

Inspection of the Posterior Wall of the Larynx.—Various devices have been employed from time to time in order to expose the posterior wall of the larynx to inspection, the foreshortening of its image in the ordinary method of laryngoscopy often preventing due appreciation of existing lesions.

The latest device is by DR. MERMOD, of Iverdon (*Annales des Maladies de l'Oreille, du Larynx, etc.*, 1898, No. 2). This consists in the use of a second mirror, which is placed within the cavity of the larynx, and which he appropriately calls a laryngendoscope. Its reflecting surface is directed toward the reflecting surface of the ordinary mirror. A small, heart-shaped mirror, movable upon its shank and controlled by a screw, is attached to the extremity of a laryngeal handle of the ordinary curve.

The illumination must be good in these cases, because the image has to be reflected from one mirror upon the other.

Transmission of Diphtheritic and Scarlatinic Sore-throat.—DR. FRANCIS T. BOND has had his attention called (*British Medical Journal*, 1898, No. 1831), by a very intelligent mistress of a board school in his district, to a practice which obtains, in infant schools especially, and which he thinks is accountable for a good deal of obscure communication of the disease. It is

that of children licking their slates for the purpose of cleaning them, and he states that a more effective way of diffusing the infection could hardly be designed.

Pharyngitis Herpetica Associated with Menstruation.—Dr. Lewis S. Somers reports (*Philadelphia Medical Journal*, February, 1898) a case of this character in which the entire mucous membrane of the buccal cavity and the pharynx was inflamed, the ulcers being extremely painful, while the nasal passages did not show any evidence of the disease. The case was treated successfully merely on hygienic principles, boric acid and honey being used locally.

"The Physiological Relations Between the Nose and the Sexual Apparatus of Man and Woman Also.—Dr. John Noland Mackenzie, Baltimore, elaborates (*Johns Hopkins Hospital Bulletin*, 1898, No. 82) his essay published in The American Journal of the Medical Sciences, April, 1884, in a paper before the British Medical Association at its last meeting in Montreal; and reference is made to a number of articles which have appeared since his own. The essay presents attractions for the curious as well as for the studious."

The Relationship of Nasal Diseases to Insanity is elaborated by Dr. C. Ziem in the *Monatsschrift für Ohrenheilkunde*, 1897, Nos. 11 and 12, and consists largely of the subject as manifested in his own person, with a summary of observations of others, and general remarks, historical, physiological, and pathological.

Congenital Occlusion of the Posterior Nares.—Dr. J. Payson Clark reports (*Boston Medical and Surgical Journal*, February 24, 1898) a case of complete congenital occlusion of the posterior nares, and gives a summary of Hubbell's collation of seventeen cases in 1886, to which he adds three additional. His own patient was a girl aged eighteen years, with an osseous occlusion, a portion of which was removed with the trephine. An illustration is given of the microscopic appearance of the thickest portion of the bone removed with the trephine.

The Asch Operation for Deviations of the Cartilaginous Nasal Septum.—Dr. Emil Mayer, of New York, reports (*Medical Record*, February 5, 1898) the result of two hundred instances of this operation, which he describes in detail, with illustrations of the instruments used. It will be remembered that this operation essentially consists in cross excision through the septum, and then in turning the four flaps thus made down upon themselves in the more capacious passage, taking care to break the cartilage so as to destroy its resiliency and keeping the weakened septum in the middle line by the agency of a perforated plug in the narrow passage. Of the one hundred and twenty-two patients operated upon in the New York Eye and Ear Infirmary, and tabulated, all are reported cured. The same is to be inferred of the seventy-eight cases operated at the Manhattan Eye and Ear Hospital which are untabulated.

[This operation of Asch is certainly the most successful with which the compiler is acquainted, and the section of the cartilage may be performed with the knife in the absence of the specially devised cutting scissor-pliers. An unfortunate sequel which has occasionally occurred in the compiler's practice is not to be ignored, and this is the sloughing of one of the flaps forcibly turned down, presumably from disturbance in its nutrition. This will leave a permanent perforation of the septum. It occurs but rarely, but the possibility of its occurrence must be duly weighed by the operator.]

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE; PROFESSOR OF OBSTETRICS AND DISEASES OF INFANCY IN THE PHILADELPHIA POLYCLINIC; CLINICAL PROFESSOR OF DISEASES OF CHILDREN IN THE WOMAN'S MEDICAL COLLEGE; VISITING OBSTETRICIAN TO THE PHILADELPHIA HOSPITAL, ETC.

Vitelline Placenta in the Human Subject.—In the *Scottish Medical and Surgical Journal*, May, 1898, BALLANTYNE concludes an interesting paper on this subject with the statement that in the sympodial fœtus it is common to find the absence of the allantois and parts derived from it. The placenta is developed from vitelline vessels with the umbilical cord. The fœtal part of the placenta has been supplied with vessels from the vitelline circulation.

The Bacterium Coli Commune as a Cause of Puerperal Fever.—In the *Archiv f. Gynäkologie*, 1898, Band lv. Heft 2, SCHENK reports two cases in which the bacterium coli commune was isolated, and by inoculation proved to be the cause of puerperal septic infection. The first case was that of a multipara on whom a midwife had produced an abortion. This patient died of sepsis. An examination showed streptococci and the bacterium coli commune to be present in the peritoneum of the patient. The second case recovered, but this germ was found in the cervix, and animals inoculated with it became septic. This germ alone is sufficient to cause sepsis, but is especially deadly when combined with streptococci. It usually finds its way into the vagina from the rectum, and hence any method of conducting labor which requires the introduction of the finger into the rectum is not advantageous.

Management of Normal Labor.—In the *Scottish Medical and Surgical Journal*, May 1898, JARDINE, in a paper on this subject, gives the following hints of practical value: As an aid to cleanliness, he would have a canvas lining for the obstetric bag, which could be removed and washed. He uses a long curved glass douche-tube, grooved for the purpose. He is careful to cleanse his hands before palpating the abdomen. Lysol is his favorite antiseptic. In supporting the perineum he pushes the whole structure forward with the extended hand. If the placenta is not removed in one half hour he introduces

the hand and takes it away. He examines the perineum immediately after birth, and sews it at once if it is torn. He considers a pulse over 100 as threatening bleeding. If a primipara has after-pains, something has been left in the uterus. He relies especially on the pulse as an indication of a good convalescence. He allows the patient to get on her hands and knees to micturate as early as possible.

A Case of Tetany in Pregnancy Following the Removal of Goitre.—In the *Archiv f. Gynäkologie*, 1898, Band lv. Heft 2, MEINERT reports the case of a multipara who developed tetany after the removal of goitre. The case became so severe that it was necessary to interrupt pregnancy, after which the patient made a slow recovery. Interesting trophic lesions accompanied the disease.

The Value of Alcohol as a Disinfectant.—In the *Centralblatt f. Gynäkologie*, 1898, No. 18, GOENNER reports the results of experiments to determine the practical value of alcohol as an antiseptic and disinfectant. His experiments were made by cleaning the hands in various ways, and then removing with an ivory nail-cleaner material from beneath the nail, and infecting animals with this material. His experiments showed very plainly that alcohol is much inferior to bichloride of mercury as an antiseptic, and is able to destroy the less virulent bacteria. Streptococci and other active germs and also spores of bacteria are not affected. He advises the use of alcohol in connection with thorough washing in soap and hot water and brushing in bichloride of mercury solution.

Ectopic Gestation and Eclampsia.—In the *Centralblatt f. Gynäkologie*, 1898, No. 18, a case is cited reported in a Norwegian journal by HOLST. The patient was a primipara, and the abdominal tumor was as large as a seven-months' pregnancy. Eclamptic convulsions were subdued by injections of morphia. It was, however, impossible to induce labor by the usual means. After two days' illness the convulsions passed away, and the patient became conscious and felt the movements of the child. She recovered and went about as usual. A month afterward fœtal movements ceased and the tumor was smaller. Five months after the eclamptic outbreak a fistula formed in the vagnia and another near the umbilicus, through which fœtal bones were expelled. A fistula connected with the bowel, but finally closed, and nine months after her illness the patient entirely recovered.

A Second Cæsarean Section for Highly Contracted Pelvis.—In the *Centralblatt f. Gynäkologie*, 1898, No. 19, BRAUN-FERNWALD reports the case of a patient with highly contracted pelvis on whom he had performed a cœlio-hysterotomy some years previous. The patient returned a few months pregnant, and at her desire, and because the pelvis was highly contracted, the pregnancy was terminated. She afterward returned pregnant near term, and it was decided to operate by cœlio-hysterectomy.

The wall of the abdomen and of the uterus was excessively thin. The silk stitches of the first operation remained, although no scar was present. The incision was made across the fundus and the child easily removed. It died

on the following day from weakness. The broad ligaments were ligated, the cervical arteries tied, the uterus amputated, and the stump stitched over. Two strands of iodoform gauze were passed down to the stump for drainage. The patient made a good recovery and the result of the operation was very satisfactory.

[We do not find it necessary to employ drainage in these cases, as under ordinary circumstances the patient is not septic and recovers promptly without a drain.—ED.]

Facial Paralysis in the Child Following its Spontaneous Birth.—At a recent meeting of the Obstetrical Society of Vienna (*Centralblatt f. Gynäkologie*, 1898, No. 19), SCHUTZE reported the case of a child born in spontaneous labor who had facial paralysis, which was found upon autopsy to depend upon hemorrhage at the base of the cranium and pressure on the cortex. A depression was found on the left parietal bone, and the scalp showed the effects of severe pressure.

Incomplete Rupture of the Uterus in Placenta Prævia.—At a meeting of the Obstetrical Society of Vienna SCHUTZE also reported (*Centralblatt f. Gynäkologie*, 1898, No. 19) a case of placenta prævia in which it was necessary to immediately make version to stop a severe and prolonged bleeding. The os and cervix would admit but three fingers, but the cervix was very soft and the version was readily made. A half hour afterward the child was easily born. Very severe hemorrhage followed the expulsion of the child and placenta which could not be checked sufficiently early to rescue the patient.

On examination, an incomplete rupture of the uterus was found, and also a partial separation of the pubic joint and increased mobility of the left sacro-iliac joint. The tear in the uterus began at the cervix.

In discussion it was brought out that special danger exists in placenta prævia of uterine rupture, because the cervix and lower uterine segment are always very greatly softened.

Posterior Positions of the Occiput and Presentation of the Parietal Bone.—In the *Monatschrift f. Geburtshülfe und Gynäkologie*, 1898, Band vii. Heft 5, MUELLER concludes an extensive paper on this subject as follows: He distinguishes three posterior positions of the occiput, right, left, and sacral. The two former in most cases end in spontaneous rotation to the front. Occasionally some other presentation develops. It is possible for birth to occur by the forehead pivoting under the pubes and the occiput being forced out over the perineum. It is important to recognize the difference between a presentation of the parietal bone and a posterior rotation of the occiput. Sacral rotation of the occiput is rare. Labor is prolonged in these cases, and laceration of the pelvic floor is inevitable. It is possible, however, in most cases to deliver the patient with forceps, although mother and child will undergo severe pressure during labor. Fortunately over 96 per cent. of all cases terminate in spontaneous anterior rotation.

Pregnancy in Fibroid Uterus, with Double Uterus in Addition.—In the last report of the Rotunda Hospital, *Dublin Journal of Medical Sciences*, May,

1898, is found a description of an interesting case of pregnancy in fibroid uterus. Abdominal section was performed and a living child delivered. Clamps were placed on the broad ligaments and the cervix was removed through the vagina. Amputation of the fibroid uterus was first performed.

A large mass of tissue was found outside the clamp on the left side. It was drawn down, another clamp placed outside, and this was removed, when it was found to be a second uterus. The patient made a good recovery.

Dangers and Treatment of Dry Labor.—BRODHEAD, *Medical Record*, May 14, 1898, describes well the dangers to mother and child arising from pressure in dry labor. He urges early interference, so soon as disturbances of the fœtal pulse occur. He has found, to bring on labor, the following treatment useful: A large dose of castor oil and glycerin, followed shortly by 10 grs. of sulphate of quinine repeated every three hours with $\frac{1}{30}$ gr. of sulphate of strychnine every two hours, careful watch being kept for unpleasant effects. He calls attention to the value of lysol as an antiseptic in these cases.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

W. T. COUNCILMAN, M.D.,

SHATTUCK PROFESSOR OF PATHOLOGICAL ANATOMY, HARVARD UNIVERSITY.

AND

F. B. MALLORY, M.D.,

ASSISTANT PROFESSOR OF PATHOLOGICAL ANATOMY, HARVARD UNIVERSITY.

Recent Work on the Toxin and Antitoxin of Tetanus.—F. BLUMENTHAL (*Zeitschr. f. klin. Med.*, 1897, Bd. xxxii.), by inoculating animals with the spinal cord and organs of four cases of fatal tetanus, produced tetanic symptoms and death. As the result of his experiments he concludes that two substances capable of producing tetanic convulsions are present in the organs of individuals dying of tetanus. One of these corresponds in its action to the filtrate of bouillon cultures of the tetanus bacillus (tetano-toxin); the other, which he calls the "organ" poison, he believes to be formed by a union between the tetano-toxin and the protoplasm of the tissue cells. The tetanus antitoxin neutralizes the former, but has little effect on the latter. Thus, if the "organ" poison is present in large amount, the administration of tetanus antitoxin is of little value, because the antitoxin neutralizes only the tetano-toxin.

METCHNIKOFF (*Annales de l'Institut Pasteur*, November, 1897, "Recherches sur l'Influence de l'Organisme sur les Toxines") considers the laws which regulate the production of antitoxins. He arrives at the following conclusions: (1) The animal organism only is able to produce antitoxins. Lower forms of vegetable life, such as bacteria and yeasts, may destroy toxins or transform the infectious organisms into vaccines, but never cause the formation of antitoxins. (2) Invertebrates cannot produce antitoxin, as is shown

by experiments on arthropodes (scorpion and larves de l'Orycites nasicornis), which when inoculated with tetanus toxin and left at a temperature of 32° C. produced no appreciable amount of antitoxin during a period of six months, though in the case of the scorpions the toxin appeared in the blood and was found to be stored in the liver in considerable quantity. (3) The production of antitoxin in vertebrates begins in the crocodile, in which animal this power is more marked than in mammals. Of cold-blooded animals the carp and the frog, if kept at a low temperature, will resist large quantities of tetanus toxin, but the toxin remains stored up in the blood for months without losing its power to produce tetanus if injected into guinea-pigs. If, however, the temperature of the animals is raised to 30° C., fatal tetanus occurs in the case of the frog, carp, or axolotl. Young alligators at 30° C. resist a dose of toxin sufficient to kill 6000 mice, and after two months their blood is decidedly antitoxic. In older animals the antitoxic power appears sooner than in younger animals—*e. g.*, the blood of an alligator weighing 4900 grammes, injected with a dose of toxin sufficient to kill 600,000 mice, after eight days showed itself to be antitoxic in a dose of 0.005 c.c. If kept at a temperature of 20° C. the alligator does not produce antitoxin. (4) In the study of warm-blooded animals he found that in the fowl antitoxic power was produced without any rise of temperature, but with marked leucocytosis. This would indicate that the production of antitoxin is not necessarily associated with febrile reaction. (5) Experiments with the blood and various organs show that, in the fowl at least, the antitoxin is stored up in the blood only, and, with the exception of the genital glands, is not localized in the organs. The antitoxic power of the genital glands is greater than that of the blood. Pericardial and peritoneal exudates of guinea-pigs are strongly antitoxic, showing that most of the antitoxin is in the fluids of the body. (6) The experiments with the lower forms of animal life (where no antitoxin is produced) make it impossible to accept the idea that immunity depends on a natural antitoxic power. (7) The evolution of the antitoxic power in the animal kingdom is more recent than the property of phagocytosis.

WASSERMAN and TAKAKI (*Berl. klin. Wochenschr.*, 1898, No. 1, "Ueber Tetanusantoxinische des normalen Centralnervensystems"), as the result of experiments, consider that the brain and cord of the guinea-pig have always an antitoxin action to the tetanus toxin which other organs of this animal do not have. They made an emulsion of the brain and cord in physiological salt solution, and added an amount of tetanus toxin several times the fatal dose. This mixture inoculated into animals produced no tetanic symptoms. Liver, spleen, kidney, bone-marrow, and blood-serum of the guinea-pig treated in the same manner did not have the same antitoxic power. The antitoxic power of the brain was always more marked than that of the cord. The fluid of the ventricles did not have this power. The central nervous system of the dove, horse, dog, and man was also found to have an antitoxic action.

A. MARIE (*Annales de l'Institut Pasteur*, "Sur les Propriétés Antitétaniques des Centres Nerveux de l'Animal Sain") reports some work along the line suggested by Wasserman and Takaki. He found the cord to be more antitoxic in its action than the brain, and that portions of the central ganglia were less active than the cortex. He does not believe that the normal nerve centres

are antitoxic in the true sense of that word, but that their action is due to an intimate union between the toxin and the emulsified brain which renders the toxin inert. To prove this theory he inoculated the toxin and the cerebral emulsion separately—for example, the toxin in the fore-paw and the emulsion in the hind. In all cases the animals died of typical tetanus. If, however, the toxin and the emulsion were inoculated together the animal recovered. This he considers to indicate that the brain emulsion acts by direct contact, for if its action is antitoxic in the true sense of the word, it would become diffused, as does the antitoxic serum, and counteract the toxin even when inoculated separately.

METCHNIKOFF (*Annales de l'Institut Pasteur*, "Sur l'Influence de l'Organisme sur les Toxines," deuxième mémoire) confirms the experiments of Wasserman and Takaki, that an emulsion of the brain of a guinea-pig in salt solution mixed with tetanus toxin produced no results on inoculation. The brain of the turtle and of the fowl have but a slight action, merely retarding the appearance of symptoms and making the progress of the disease more chronic. The cord has no action. These animals are but slightly sensitive to tetanus, while the guinea-pig is exceedingly sensitive. From these facts he concludes, therefore, that animals exceedingly sensitive to tetanus have an antitoxic power in a high degree, while animals refractory to tetanus have little or none. The brain of frogs, however, which are extremely sensitive to tetanus, has absolutely no antitoxic power, even when the animal is kept at a temperature of 37° C., a fact which leads him to consider this property to be limited to mammals. In studying the comparative antitoxic power of the blood and of the central nervous system he found the blood much superior to the brain. On removing a portion of the cerebral hemisphere the antitoxic power of the blood was doubled in a few days. After seventeen days, however, the power of the blood and brain was equal. Of all the other internal organs—liver, spleen, kidney, muscles, bone-marrow, and ovaries—the latter had the greatest antitoxic power. These results do not indicate that the nervous system is the source of antitoxin production.

For the purpose of comparing the antitoxic power of the liquids of the body with that of the organs, he produced, by the inoculation of 10 c.c. of physiological salt solution into the peritoneal cavity, a peritoneal exudation. This exudation, which contained 118,000 leucocytes per c.mm., had an antitoxic power twice that of the normal blood. The pericardial exudation had an antitoxic action less than that of either the blood or the peritoneal exudation. The brain and cord had an antitoxic power one-tenth that of the blood or peritoneal exudation. The internal organs—liver, spleen, kidneys, suprarenal capsules, and bone-marrow—had an action more marked than that of the brain and cord, but less than that of the liquids. Of the organs, the kidney had the strongest action, and the spleen and bone-marrow the least. From these observations he concludes that the central nervous system is not the seat of production or the point of accumulation of the antitoxin. He does not accept the conclusion of Wasserman and Takaki, that the protective action of the normal nerve centres of the guinea-pig is due to an antitoxic action. He refers to the work of Marie, but does not agree with his theory that the toxin is destroyed by the direct action of the cerebral mixture. For if this were the case, tetanus could be as easily cured in the

guinea-pig as in the mouse; but it is not. He considers the essential thing to be an increased production of leucocytes by the organism itself, as a result of the inoculation of the toxin and brain mixture. This theory he illustrates by injecting into the anterior chamber of the eye of a rabbit some tetanus toxin which produces little or no reaction. If, however, with the toxin he inoculates a portion of the cerebral tissue an intense inflammation is produced which leads to hypopyon. This reaction is much more marked than that produced by cerebral tissue alone. The immunity, therefore, is due to the leucocytosis produced by the injection of this mixture of toxin and brain; for leucocytes have the power not only to destroy bacteria, but also to destroy and alter toxic substances.

BEHRING and RANSOM (*Deutsche med. Wochenschr.*, March 24, 1898, "Ueber Tetanusgift und Tetanus Antitoxin"), as the result of experimentation, find that, when the antitoxin is added to the toxin in sufficient amount exactly to neutralize it, no symptoms are produced in animals inoculated with the mixture. In all cases in which the toxin is in excess the animal dies. An excess of toxin may be so dilute, however, that the animal recovers. It appears, therefore, that the antitoxin renders inert a definite amount of toxin, and that the toxin left over is still active.

An examination of various organs of the animals which succumb shows the toxin to be present in varying amount. The body viscera show the greatest amount, while none is found in the brain.

FERDINAND BLUMENTHAL (*Deutsche med. Wochenschr.*, March 24, 1898, "Ueber die Veränderung des Tetanusgiftes im Thierkörpers und seine Beziehung zum Antitoxin") discusses the finer changes in the nerve-cells resulting from the union with the toxin, and makes the point that these changes are not mechanical but chemical. This theory would explain those cases in which the injection of antitoxin produces no effect, for it can combine only with the toxin circulating freely in the blood and not with that which is already chemically combined with the cells.

F. RANSOM (*Deutsche med. Wochenschr.*, February 24, 1898, "Das Schicksal des Tetanusgiftes nach seiner intestinalen Einverleibung in den Meerschweinorganismus"), as the result of intestinal inoculations of tetanus toxin in guinea-pigs, finds that even in very large doses it produces no effect on an intact gastro-intestinal mucous membrane. It is not absorbed by either stomach or intestine, because neither toxin nor antitoxin appear in the blood. The toxin is finally excreted unchanged with the feces.

METCHNIKOFF (*Annales de l'Institut Pasteur*, April, 1898, "Recherches sur l'Influence de l'Organisms sur les Toxines (troisième mémoire), Toxine Tétanique et Leucocytes") reports further work in support of the theory of the destruction of toxins by leucocytes. He refers to the fact that as every bacterium contains some toxin, a cell taking up this bacterium must have some means of altering the toxin as well as destroying the bacterium. This absorption and destruction of tetanus toxin by leucocytes has been demonstrated by him in the fowl. Injection of toxin into a fowl or guinea-pig is always accompanied by a marked leucocytosis. Still further to strengthen his theory, he inoculated animals intraperitoneally with an emulsion of brain-substance mixed with tetanus toxin. Fluid withdrawn after twenty minutes showed large numbers of macrophages filled with brain-substance, while

practically no brain-substance could be found lying free. As the toxin is known to adhere to the brain-substance it must be assumed that the toxin also is absorbed by the cell. In these cells the toxin probably undergoes some change by digestion, or possibly oxidation, which renders it inert.

ROUX and BORREL (*Annales de l'Institut Pasteur*, April, 1898, "Tétanos Cérébral et Immunité contre le Tétanos"), by direct inoculation of tetanus toxin into brain-substance, produced, instead of the permanent contractures of ordinary tetanus, epileptiform crises, excitation, polyuria, and motor disturbances, forming a group of symptoms with distinct characteristics. By injection into different parts of the brain, different groups of muscles may be affected, an experiment of considerable physiological interest.

Experiments on a large number of animals showed that intracranial injections of antitoxic serum were much more efficacious for ordinary tetanus than subcutaneous injections.

That the brain-cells have not the power of storing up or producing antitoxin was shown by the fact that an immune animal did not react to a subcutaneous inoculation of toxin, but did to an intracranial inoculation. If the brain-cells contained an antitoxin they would have been able to counteract the toxin.

The resistance to tetanus in immune animals is not due to the fact that cells, particularly nerve-cells of the brain, become accustomed to or are insensible to the toxin; but to the fact that the toxin does not reach the brain. The toxin is intercepted and retained by other cells of the body which exercise a protective rôle and probably manufacture antitoxin. These cells are probably phagocytic cells. In all probability immunity against bacteria and against toxins will yet receive similar explanations.

MORAX and ELMASSIAN (*Annales de l'Institut Pasteur*, March 25, 1898, "Action de la Toxine Diphtherique sur les Muqueuses") find that the instillation of pure diphtheria toxin into the normal conjunctival sac of rabbits produces lesions identical with those produced by the diphtheria bacillus. The instillation was kept up for eight or ten hours, and the results appeared in from thirty-six to forty-eight hours. A dilute solution, 1 part of toxin to 4 of normal salt solution, was used. (It is hardly appropriate to speak of the conjunctiva or cornea at the end of the process of instillation as normal. No cultures from the inflamed conjunctiva are mentioned.)

V. BABES (*Berliner klinische Wochenschrift*, January 3, 1898, xxxv., No. 1, on the "Influence of Different Infections on the Nerve-cells of the Spinal Cord"). The nervous symptoms of severe infectious diseases, such as typhoid fever, diphtheria, etc., usually pass off without leaving any noticeable permanent effects. Nerve-cells, however, regenerate very slowly, and it is thought by many that complete restitution never takes place. It has been noted that many nerve-cells of adults after recovery from diseases affecting the nervous system are abnormal. The number of such altered cells could be taken as evidence of whether or not there were any symptoms of nervous disease during life.

In the old are found atrophic cells, homogeneity of the cells, a large quantity of pigment, probably arising from destruction of chromatophilic elements and lying usually in a preformed substance, which, in the form of small hyaline bodies, is arranged in masses or scattered through the cell-bodies,

even extending into the axial portion of the process. In cells of certain regions (Clarke's column, parts of the anterior horn, certain nuclei of the bulb) is often found a homogeneous mass arising from changes in the cell-substance (œdema or hyaline metamorphosis), and the nucleus is pushed to the periphery. Sometimes there is pigment in the cell. Often the processes are indistinct. One may find in a group of relatively intact cells shrunken colloid or very pale elements with processes lost and nothing left of the nucleus but the nucleolus. The chromatophilic granules are pale or wholly lacking in the periphery of the cell, while they are more numerous around the nucleus. Cells with a large vacuole around the nucleus often occur. Occasionally one finds a cell which lies in a large space containing leucocytes, small epithelioid cells, pigment granules, or even chromatophilic granules or a nucleus extruded from the cell. In young children these changes are not found, with the exception of the heaping up of the chromatophilic elements about the nucleus or in a circumscribed part of the cell. The absence of any of these changes in many cases is to be explained, probably by the greater resistance of the cells, as we know that not only the cells of different individuals but also the cells of different parts of the nervous system of the same individual vary in this power of resisting injury. In animals inoculated with cholera and other infectious diseases and killed some weeks after recovery, more altered cells were found in the anterior horn than in those of non-infected animals. In typhoid fever, pyæmia, septicæmia, and scarlet fever changes were observed in the anterior horn consisting of the proliferation of cells around the vessels, of small hemorrhages, and of the presence of minute micro-organisms in the central canal and around the vessels. These changes had for site of predilection the capillary plexuses around the nerve-cells. The cells themselves showed a rarefaction of the chromatophilic substance which was becoming diffuse and vacuolated, or else a sort of coagulation of this substance, with staining of the nucleus, but not of the nucleolus. Sometimes there was a sort of œdema with vacuoles in the cell. Micro-organisms were found in considerable numbers in the central canal and anterior horns of cases in which there were no nervous symptoms.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

EDWARD F. WILLOUGHBY, M.D.,

OF LONDON,

AND

CHARLES HARRINGTON, M.D.,

INSTRUCTOR IN MATERIA MEDICA AND HYGIENE, HARVARD MEDICAL SCHOOL.

Meat-poisoning: "Botulismus."—Much light has recently been thrown on the subject of meat-, sausage-, and fish-poisoning as a result of careful research growing out of a remarkable set of cases occurring at Ellezelles, in Belgium, reported by PROF. E. VON ERMENGHEM (*Zeitschrift f. Hygiene und Infectionskrankheiten*, xxvi. p. 1). Over twenty members of a musical society

were seized with serious illness after eating the greater part of a raw pickled ham; three died within a week, and ten were in a critical condition. Other parts of the animal from the same pickling tub were eaten in a raw state without ill effects, and pieces of the particular ham had been consumed a short time before, also without results. Only those persons who ate of the ham were taken with the very peculiar train of symptoms recorded. Most of them were seized in from twenty to twenty-four hours, three in less than that time, and a few as late as thirty-six hours after eating. The first symptoms were gastric pain, nausea, and vomiting of undigested food and gelatinous blackish matters. Instead of diarrhœa, which one would expect, there was obstinate constipation in all but two cases, and the first dejections with or without cathartics were black and viscid. In every case in from thirty-six to forty-eight hours there was profound disturbance of vision: amphodiplopia; marked dilatation of the pupils, with absence of reaction to light; ptosis of both lids, and a peculiar fixed stare. There were burning thirst and a strangling sensation in the throat. Swallowing, even of liquids, was difficult or impossible, and every attempt was accompanied by decided choking. The mucous membranes of the mouth, nose, and pharynx were much reddened, and were coated with gray, thick mucous masses, which, accumulating, caused distressing cough and choking. In some instances the saliva was suppressed and the mucous membrane dry and glossy. The voice was weak, and with some there was total aphonia. Dysuria and anuria were common. There was but little disturbance of respiration and circulation; the pulse never reached over ninety, respiration was quiet, temperature normal. Consciousness and general sensibility remained intact throughout, except in the fatal cases, in which alone several hours before death there occurred collapse, dyspnœa, small irregular pulse, light delirium, and coma.

There was obstinate insomnia in many during the first period. The extremities and trunk-muscles showed neither complete paralysis nor atrophy, but there was great general muscular weakness, and slight movements caused extreme fatigue. After two or three weeks the eye symptoms began to improve. The dilated pupils began to contract, the cloudiness to disappear, and the half-paralyzed eyelids to regain their power. Diplopia disappeared only when both eyes were fixed laterally. Paralysis of accommodation lasted a long time after the disappearance of all the other symptoms, and normal vision did not wholly return until after six to eight months.

Autopsy in two cases showed no characteristic changes in the organs, only remarkable hyperæmia of the kidneys, liver, and meninges, and softening and extraordinary friability of the stomach-walls. In one the liver showed marked degeneration, and the brain punctiform hemorrhages. Neither the liver nor kidneys showed anything unusual on bacteriological examination, but the spleen yielded an anaërobic bacillus which proved later to be related to Botulismus.

The pig from which the ham came was killed some months previously, and what was not eaten at once was pickled in the usual way. During the time that elapsed between the pickling and this occasion the greater part of the animal had been consumed without causing any sickness, but the ham which, nearly intact, was the last to be eaten, lay on the bottom of the tub, and was the only part that was completely immersed in the weak brine. What

was left of it gave off no odor of putridity, but had a distinct odor like that of rancid butter. That the ham had a bad taste was agreed by nearly all who ate of it. It appeared normal to the eye, but was pale like any meat which has been soaked some time in water. There was no evidence of decomposition, and neither ptomaïnes nor other poisonous alkaloids were present.

Bacteriological examination proved in different parts the presence of a hitherto unknown spore-bearing bacillus in great abundance, the same organism as that isolated from the spleen of one of the victims. It produces an extraordinary virulent toxin which was isolated by Brieger from cultures supplied by the discoverer, by whom the organism was named Bacillus botulinus. The toxin is rendered inert by a temperature of 60° to 70° C., therein agreeing with other bacterial toxins thus far isolated, and differing from the cause of ordinary meat-poisoning from cooked meats.

Attempts to discover the organism in the feces of various animals and in filth of various kinds, and in specimens from where the pig was raised, were negative in results.

Feeding-experiments conducted on various kinds of animals with the meat itself and with aqueous triturations of it added to other foods, produced, as a rule, fatal results with the same train of symptoms as above mentioned. Subcutaneous injections of the watery extract produced the same results as feeding-experiments.

The aqueous extract in a sealed tube kept in the dark retained its strength unimpaired for ten months, and small pieces of the meat kept in cotton-stoppered tubes without any special precautions retained their original virulence even longer. The poison resists the effects of putrefaction, and proved to be equally poisonous after four days' standing mixed with feces, decomposing blood, and urine, and filtration through porcelain. A fresh filtrate, to which were added *B. prodigiosus*, *B. proteus liquefaciens*, *B. fluorescens putridus*, and *B. coli*, was found at the end of a week to be as active as ever.

Prof. Brieger and Dr. W. Kempner (*Deutsche medicinische Wochenschrift*, 1897, No. 33) succeeded in isolating the active poisonous principle from cultures of the *B. botulinus*, and proved it to be closely related chemically to the toxins of diphtheria and tetanus. Next, Kempner (*Zeitschrift f. Hygiene und Infectionskrankheiten*, xxvi. p. 481) undertook to examine into the subject of immunity to the toxin, employing bouillon cultures killed by the application of toluol, culture filtrates free from bacteria, and the concentrated and purified poison, the strength of which was accurately determined with guinea-pigs. The first experiments in immunizing guinea-pigs and rabbits proved that with them active immunity cannot be attained even when beginning with the smallest possible dose, as in every case, after a shorter or longer interval, every animal perished. With goats it was found that immunity could be conferred by continued increasing subcutaneous injection, and that the serum of the immunized animal possesses a very high protective power, as is shown by the fact that prevention is accomplished by injection performed thirty hours before the introduction of the poison, and that it is manifested also by direct application in the stomach of cats poisoned by the mouth. It was found also that the antitoxin would cure guinea-pigs when administered twenty-four hours after inoculation with a dose which would be fatal ordinarily in forty-eight, and even when decided clinical signs of poisoning were already present. Later, Kempner and Dr. E. Schepilewsky

(*Zeitschcift f. Hygiene und Infectionskrankheiten*, xxvii. p. 213) began a research on the possible affinity of nerve-substance for the botulismus toxin which, as shown by clinical symptoms and pathological examination, exhibits a decided tendency to certain points of the central nervous system. The test poison was so standardized that 0.000,005 c.c. represented twice the dose necessary to kill white mice of 15 grammes weight in from two to three days. The brains of freshly killed guinea-pigs were rubbed finely with physiological salt solution in the ratio of 3.3 grammes to 10 c.c., and the cords were treated in a similar manner. Both emulsions were practically neutral in reaction. Pieces of the liver, kidney, spleen, muscles, and marrow were treated in the same way, to be used for comparison. In the first series of experiments, 1 c.c. of the brain or cord emulsion mixed with three to four times the fatal dose of the toxin was injected under the skin of a number of mice, and as controls other mice were injected with the same amount of toxin alone, and others with the toxin mixed with the emulsions of the other organs. The results showed that the brain and cord do possess and exert a decided preventive and curative influence, and that the other organs do not. With mixed injection it was always possible with 1 c.c. of the emulsion to counteract three times the fatal dose, while with four times the dose about half the animals died. With separate but simultaneous injections only about half of the animals would survive twice the fatal dose, the others dying about as quickly as the controls. As a curative agent in cases where the poison had been exhibited six and twelve hours previously, the emulsions did not give such favorable results, for those treated after twelve hours died as soon as the controls, and the others lived but a day longer.

Whatever the protecting substance may be, it was proved that it is in combination with nerve-substance and insoluble in water; its influence is materially altered by high temperatures, but not by keeping several days in ice.

Milk, butter, yolk of egg, and other animal fats were tried in the same way, but no results were obtained, excepting with butter, with which two guinea-pigs were protected, but which failed with other animals. A thin oil emulsion mixed with two and even four times the fatal dose was successful.

Lecithin and cholesterin, substances normally present in nerve-substance, proved to have antitoxic power, which was unimpaired by boiling or heating; but quite large amounts were necessary. Other substances, as cerebrin, nuclein, and bile, proved to be inert, but antipyrin in larger amounts than 0.10 gramme (0.15 to 0.20) proved able to neutralize 0.000,003 c.c. of the toxin. Given in doses of 0.10 gramme, antipyrin had no effect, the animals dying at the same time as the controls; but if the animals had been first treated with antipyrin as a preliminary measure the above dose would act.

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All communications should be addressed to

DR. EDWARD P. DAVIS, 250 South 21st Street, Philadelphia, U. S. A.

Or

DR. HECTOR MACKENZIE, 59 Welbeck St., Cavendish Sq., London, W., Eng.

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